THE INTERPRETATION OF DEVELOPMENT AND HEREDITY

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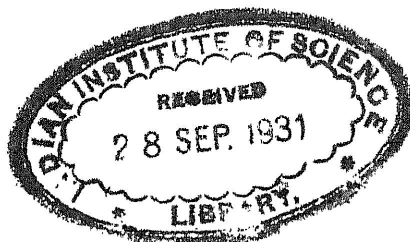
THE INTERPRETATION OF DEVELOPMENT AND HEREDITY

A STUDY IN BIOLOGICAL METHOD

BY

E. S. RUSSELL

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'He said that new systems of nature were but new fashions, which would vary in every age; and even those who pretend to demonstrate them from mathematical principles would flourish but a short period of time, and be out of vogue when that was determined.'

JONATHAN SWIFT.

'Allein die Natur giebt dem Beobachter derselben nur Stoff zur Bewunderung der Einfachheit, mit der sie wirkt, und zur Verwunderung über die Geneigtheit, mit der der menschliche Witz ein ihm wunderbar scheinendes Phänomen durch unendlich grössere und unbegreiflichere Wunder erklärt.'

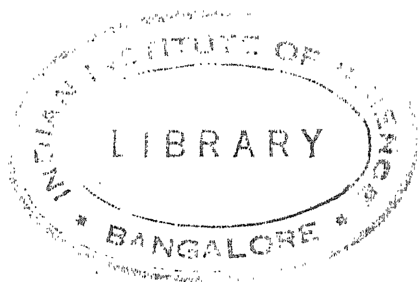
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PREFACE

I DESIRE to express my thanks to my friends Professor A. E. Boycott and Mr. G. W. Harris for their critical reading of this book in manuscript, and to Mr. Harris for some of the translations from the German. I am indebted also to Mr. R. G. Collingwood for some sound advice on matters touching philosophy.

E. S. R.

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I

INTRODUCTORY

THE general problem of development is without question one of the most difficult and intriguing in the whole field of knowledge. That from a minute germ of relatively simple structure there should be gradually built up, by a series of processes beautifully co-ordinated in space and time, the complex organization of the adult is a fact that has never ceased to excite the wonder of mankind. It has provided a constant challenge to the intellect of man, and many and various have been the theories invented to explain it. It ranks as one of the major problems of biology.

A convenient classification of biological problems is that which divides them into problems of the individual and problems of diversity. The problems of the second group relate to the differences between organic forms and the mode of origin of these differences; they comprise such problems as the origin of species, and generally the factors and causes of organic evolution. The problems of the individual are those which are common to all living things and may be studied in any individual whatsoever. They relate to such organic activities as behaviour, general physiological functioning, reproduction, and development.

I propose in this book to discuss the general interpretation of development, heredity, and reproduction, considered as essential and fundamental functions common to all living things. No attempt will therefore be made to deal with the specific modalities of these functions. The discussion will relate almost exclusively to the development and reproduction of animals. What is the best way of envisaging the problems of development and reproduction; which will give us the deepest insight into them, and enable us to understand them most fully and adequately? This is the principal question with which we shall deal. Particular attention will accordingly be paid to questions of method, that is to say to the various ways in which the problems may be and have been

approached, and to the fundamental assumptions and modes of thought which lead to these various lines of approach.

It will be necessary to treat of the matter to some extent historically, in order to be able to envisage modern theories in their proper perspective, to understand their mode of origin, and generally to follow out the filiation of ideas. We shall find that, in spite of the vast accumulation of detailed knowledge, which is, in some quarters, supposed by itself to constitute science, there is much less difference than one would expect between the fundamental hypotheses or modes of explanation adopted, say, by the Greeks and those in vogue at the present day. This is because there are—apparently—only one or two possible ways of interpreting development open to the human intelligence, and these few alternative methods tend to recur again and again throughout the whole history of biological science. One is accordingly forced to the conclusion that on its constructive or theoretical side biology (and perhaps the other sciences as well) is by no means a simple transcript of fact, but in large measure a construction of the mind, a conceptual edifice, the lines and plan of which may vary according to the type of mind of its architect. The relative parts played by fact and hypothesis in the building up of biology would make a fascinating subject for detailed treatment; we shall deal with it to some extent in this book, apropos of theories of development.

We shall find in the course of our historical survey of the main types of theory regarding development and heredity[1] that one cardinal problem of method continually arises, namely, the relation of the parts to the whole. Is development to be treated as essentially an activity of the organism as a whole, or can its full explanation be found by analysing the process into its constituent elements? Is heredity essentially the reappearance and realization of the functional potentialities of the whole, or are the separate characters of the organism transmitted piecemeal, being represented separately

[1] We regard heredity as one of the main characteristics of development—see below, p. 8.

in material form in the germ? Are development and heredity functions of the organism as a whole, or functions of its cells, or of still smaller constituent units? In general, is the organism a real unity or individual, not completely reducible to its constituents, or is it a mere composite, built up as a hierarchy of independent units? Can the whole be fully explained in terms of its parts, or must the parts ultimately be explained in terms of the whole? This fundamental question, which may be thus variously and somewhat loosely formulated, is one which will occupy us throughout the book. We shall find that according to the answer given to this question theories may be classified as 'unity' theories or 'particulate' theories. We shall find the antithesis between the two views expressed quite clearly by Aristotle in his criticism of the pangenesis theory of Hippocrates and Democritus. It recurs again in the disputes between the preformationists and the epigenesists in the seventeenth and eighteenth centuries, and the battle continues even to the present day.

After our historical sketch of typical theories we shall accordingly devote some time to elucidating the contrast between these two main types of theory, to laying bare the fundamental premisses on which they are respectively based. We shall here come to grips with the fundamental problem of the relation of the parts to the whole, and with the use and misuse of the method of abstraction.

We shall find reason to conclude that although the analytic method has added greatly to our knowledge of heredity and development and indeed remains indispensable, it must be corrected and supplemented by the integrative view which is essential for the full understanding of these processes. Accordingly, after this general discussion of the two main types of theory, we shall attempt to work out and justify a particular form of the integrative view, which may best be described as the 'organismal'[1] theory of the living thing. This is a development (and I hope an improvement) of certain views on biological method which I have already

[1] The word is borrowed from Ritter; see p. 176 below.

published. It is claimed for it that it gives a less abstract and schematic account of the living thing than that offered by the mechanistic conception, with which it is contrasted, and that it opens up the possibility of a real and autonomous biology.

The remainder of the book is devoted to testing, and illustrating the use of, this organismal method, by applying it to the study of the very earliest stages of development—with particular and critical reference to the cell-theory and the chromosome-theory—and to the general interpretation of reproduction, both sexual and asexual. No attempt is made to deal in terms of the organismal theory with the special problems of development and reproduction; the great wealth of fact disclosed by the experimental work of the last few decades on the physiology of development[1] has been left for the most part untouched, though I am convinced that the application of the organismal conception to these results would be fruitful and illuminating. My primary object has been to describe a point of view, to sketch a method of approach, and to indicate the *general* conception of development and reproduction to which it leads. This is outlined in the final chapter, which draws together the threads of the argument which run through the whole book.

As a prelude to our historical survey of theories (Chapters II–VIII), it is proposed to enumerate here the main characteristics of development and reproduction. There is a certain advantage in doing this, even in a crude and elementary way, for we can only judge of the success or adequacy of a theory if we bear in mind the main and outstanding facts for which that theory must account. Furthermore, in these days of specialization one is very apt to forget or overlook the broader and simpler aspects of a complex phenomenon like development; it is worth while then to correct our too microscopic vision by taking a bird's-eye view of the problems as a whole.

[1] A useful summary of an important section of these results is given by G. R. de Beer, 'The Mechanics of Vertebrate Development', *Biological Reviews*, ii, 2, pp. 137–97, Cambridge, 1927.

(1) The most general characteristic of development is clearly the fact of increasing differentiation of structure and function. Devèlopment is essentially a progression from a simpler to a more complex organization, with a concurrent specialization and limitation of function. This holds good both with unicellular and with multicellular organisms.

Differentiation does not mean quite the same thing applied to structure as it does applied to function. There is formation of new structure during development, an actual increase in material complexity, bringing into being structures not there before. There is no such new formation of function, for all essential functions are present already in the living egg, though in an undeveloped state. The egg breathes, absorbs nourishment, grows, excretes waste products, exhibits irritability and movement of its parts; the grown organism does nothing essentially different, exception made of the function of reproduction. What happens in the differentiation of function is not new creation, but the specialization and intensification of powers already present, and their localization in special organs which permit of their full development. With this specialization of function there necessarily goes hand in hand a limitation of function, according to the principle of the division of labour.

Furthermore, the relation of function to structure differs at different periods of development, and we may follow W. Roux (see below, p. 106) in distinguishing in many forms a first period, in which the parts and organs are differentiated in advance of, and as it were, in preparation for, functioning, and a second period in which differentiation is dependent on functioning, in which functional activity, if it does not create, at least shapes and polishes the organ. We may distinguish then *non-functional differentiation* from *functional differentiation.*

While development is normally an increasing differentiation—a formation of new organized structure and an accentuation and localization of functions already present—there occurs under special conditions and in special cases the reverse process of *dedifferentiation*, as in the simplification of

structure shown by a starved Planarian or an encysted Ciliate. So, too, retrograde or degenerative development may follow initial differentiation, as in many sessile and parasitic groups. Again, the process of differentiation may restart after a phase of dedifferentiation. It is convenient then to distinguish as a first group of characteristics, differentiation, dedifferentiation, and redifferentiation, and differentiation we may subdivide into functional and non-functional.

(2) Differentiation is essentially a formation of *organized* structure, and an unfolding of *co-ordinated* functional activity. There is therefore throughout the whole course of development a *unity* or *harmony*, which expresses itself in the spatio-temporal co-ordination of its processes. The organism developes essentially as a whole, as a unitary individual, persisting in time. There is an orderly succession of events in ontogeny, one stage leading to the next, the whole series showing a deep-seated rhythm which it is very difficult to upset or reverse. At every cross-section of this spatio-temporal 'event', which *is* development, the organism is a complete and co-ordinated whole.

We shall see later that this fact of the unity, in a spatio-temporal sense, of the developing organism constitutes not so much a problem as a postulate. A continuing unity is part of the concept of organism at which we shall later arrive. It may be possible to investigate and explain the ways in which this fundamental unity of the developing organism is maintained and restored, but the fact itself is not susceptible of complete explanation, and must be accepted as an irreducible postulate of biology. It is in discussing the problem of the relation of the parts to the whole that we shall discover the inevitability of this postulate.

(3) Another striking characteristic of the developing organism is its *autonomy*. By this I mean its relative independence of environment, its self-containedness, its steady persistence towards the goal of the finished form. The developing organism acts *as if* it were fulfilling an end or purpose—that of arriving at the typical form and modes of

activity of the species; it tends towards this goal in spite of difficulties, and the end is more constant than the way of attaining it. The environment supplies the conditions for development, provides the means, and also acts as a limiting factor, but the developing organism reaches its definitive form as it were in spite of environment, utilizing environment where it can, and seeking other conditions when the environment becomes unfavourable to its development. It is impossible by experimental means to alter substantially the specificity of development; an embryo will, if the conditions are possible at all, reproduce its typical form, or as much of it as it can. Absence of essential environmental factors may prevent development altogether, or lead to the production of monstrous and non-viable forms, but alteration of environmental conditions will not produce an essentially different embryo.

The word autonomy well expresses this characteristic of development, for the embryo in a very real sense embodies and fulfils the law of its own being.

With this character of autonomy one may associate the allied characteristic of *regulation*. If the conditions do not permit of a straightforward normal development, if for instance the developing organism suffers deformation or loss of parts, it has to a considerable degree the power of so modifying the course of its development as to cope with the unusual situation, replacing, for example, the missing parts. Innumerable examples could be given of this remarkable power possessed by the developing organism of so regulating its structure and activities as to counteract adverse influences and arrive at an approximately normal result; the phenomena of regeneration occur naturally to the mind.

(4) Not only does the developing organism arrive at a typical form of organization if development is possible at all, but this typical form is an amazingly exact replica of the form of its parent or parents. This is the fact of *heredity*.

The broad fact of repetition of type has tended of recent years to become lost from sight, because of the excessive attention paid to the laws of transmission of such slight

variations or differences as are no bar to successful interbreeding; the study of heredity has come to mean in practice the study of the modes of inheritance of minor differences. But clearly there is this major problem which is practically untouched by genetic or statistical studies, and equally clearly, repetition of type must be regarded as one of the main characteristics of development, not as a separate and independent problem.

We shall accordingly treat of heredity as being primarily a feature of development; it must, however, be given almost undue prominence in our historical survey, on account of the methodological interest which attaches to the many theories purporting to explain it.

We note in passing that hereditary resemblance applies throughout the course of development; the cycle of changes undergone by the offspring is the same as it was for the parents; there is a point-for-point correspondence between equivalent stages in the development of both.

(5) Not only is the developing organism compelled to retrace step by step the course of development followed by its immediate ancestors, but it is influenced by the evolutionary history of its race, so that its development repeats in a certain measure, and in a general way, the evolution of its race. This is the fact of *recapitulation*. It has been denied by some, and there is in fact considerable uncertainty in many cases as to how far interpretation in terms of ancestral history is valid, but one has only to think of such striking examples as the transitory appearance and subsequent transformation of the gill-slits and gill-arches in Amniota to realize that recapitulation does take place, and that it must be reckoned as a general feature of development. It accounts for the curiously indirect course which development frequently takes.

Much of the uncertainty as to the extent and significance of recapitulatory processes in development arises from the circumstance that we do not know, except in relatively few cases, the actual evolutionary history of any group, and we are thus thrown back upon probabilities. The theory of

recapitulation has in the past been employed much too freely as a means of deducing probable lines of descent, and such speculations have tended to bring the theory into disrepute. But recapitulation remains all the same an important characteristic of development, and as such requires explanation.

Repetition of type and recapitulation have both to do with the all-important historical aspect of development. The organism is above all a historical being; in some way, which we do not as yet clearly understand, the past experience of the race lives on in the present activities of the individual; nowhere is this more clearly exemplified than in the course of individual development.

The above may be regarded as the main characteristics of development, which every comprehensive theory must take into account and explain if it can. There are others which might be mentioned, as for instance the fact of sexual differentiation, which is so widespread in the organic realm. A complete theory of development would have to take into account also the life-cycle as a whole, with its successive phases of youth, maturity, and old age, and not limit itself merely to the phenomena of embryonic development.

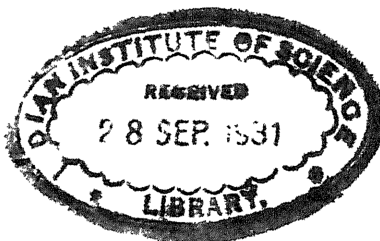
In this connexion the preparations which the organism makes for *reproduction* would require particular study—including the investigation of the later developmental processes leading to maturity, the seasonal and cyclical changes in structure and behaviour associated with reproduction, and the formation, growth, and ripening of the germ-cells.

Though good work has been done from the physiological side, reproduction has ceased to be taken seriously as a primary biological problem, ever since the general acceptance of the germ-plasm theory. In particular, the relation between sexual and asexual reproduction has rarely of late been considered with any thoroughness, nor the rationale of the long process of ripening which the germ-cells undergo. Yet reproduction is one of the master-functions of the organism, in a sense the crown and completion of individual development, and its influence on behaviour is enormous. We shall

accordingly in the last chapter devote some attention to outlining, as well as a theory of early development, the general theory of reproduction to which the organismal conception of the living thing naturally leads.

In the historical chapters which follow no attempt will be made to give a complete survey of theories; this has already been done in a thoroughly adequate way by Delage;[1] we shall consider only certain typical theories, which present points of special methodological interest.

[1] Yves Delage, *La Structure du Protoplasma et les Théories sur l'Hérédité et les grands Problèmes de la Biologie générale*, Paris, 1895, 2nd edition, 1903.



II

ARISTOTLE'S 'DE GENERATIONE ANIMALIUM'

ONLY to those unacquainted with Aristotle's treatise on the development of animals will it seem strange that in a survey of the more important theories concerning development and heredity we hark back to such early beginnings. Aristotle's biological knowledge, though remarkably extensive in its way, was hopelessly imperfect when it came to the minute study of the early stages of development; he had naturally no glimmering of an idea that the semen, which played so great a part in his theory of development, was composed of minute living organisms, the spermatozoa, nor that the female also produced, not a mere material secretion, but organized living unities, or eggs. His theory would have been transformed had he known these to us elementary and commonplace facts. He knew, and could know, nothing of the cell-theory, nor of segmentation and the formation of germ-layers. Even such incidents of early development as could be observed with the naked eye were not always noted by Aristotle with accuracy—he, like so many of us, was inclined to see what he wanted to see, and to ignore the rest —witness his inaccurate observation that the heart is the first organ to be formed in the embryonic Vertebrate. He was convinced on first principles that this must be so. As a storehouse of observed and established fact his treatise is then practically valueless at the present day.

Yet such was the sheer intellectual power of the man that he was able to work out from inadequate and largely incorrect data a theory of development which must even today be treated with respect. The form which he gave it can hardly be accepted now, but no one after him has put so much fundamental brain-work into the discussion of the central problems, and for this reason it is worth our while to consider Aristotle's ideas in some detail. We shall take first his famous analysis and refutation of the theory of pangenesis put forward by Hippocrates and Democritus.

Bear in mind that it was the general view of the ancients that the embryo was in some way formed from the semen of the male and a corresponding secretion in the female; they knew nothing of ova and spermatozoa, nor of any cellular or vital continuity between one generation and another (hence, incidentally, the idea of spontaneous generation did not seem in any way strange to them, whereas to us it is almost inconceivable). Now Hippocrates had suggested that the semen came from all parts of the body, much as in Darwin's theory 2,000 years later—how thought repeats itself!—all the parts produced pangens which were collected and stored up in the generative cells.

'The proofs', writes Aristotle,[1] 'from which it can be argued that the semen comes from each and every part of the body may be reduced to four. First, the intensity of the pleasure of coition; for the same state of feeling is more pleasant if multiplied, and that which affects all the parts is multiplied as compared with that which affects only one or a few. Secondly, the alleged fact that mutilations are inherited, for they argue that since the parent is deficient in this part the semen does not come from thence, and the result is that the corresponding part is not formed in the offspring. Thirdly, the resemblance to the parents, for the young are born like them part for part as well as in the whole body; if then the coming of the semen from the whole body is cause of the resemblance of the whole, so the parts would be like because it comes from each of the parts. Fourthly, it would seem to be reasonable to say that as there is some first thing from which the whole arises, so it is also with each of the parts, and therefore if semen or seed is cause of the whole so each of the parts would have a seed peculiar to itself' (721 b).

Aristotle deals satisfactorily with the first rather quaint argument; with regard to the second he exhibits a quite modern scepticism as to the evidence, and remarks profoundly that 'if mutilated young are born of mutilated parents, it is for the same reason as that for which they are like them' (724 a). It is, however, the third and fourth arguments that interest us particularly. We shall follow carefully Aristotle's reply to these arguments, for he deals here with quite fundamental ideas as to the *method* of explaining hereditary

[1] *De Generatione Animalium.* Translated by Arthur Platt, Oxford, 1910.

resemblance, and the discussion has direct relevance to all later theories of representative particles, and indeed to all theories postulating a particulate germ-plasm.

Should the resemblance of the whole be explained in terms of the point-to-point resemblance of the parts, or is there some fundamental cause of the total resemblance which explains incidentally the point-to-point correspondence? This is a fundamental question which is rarely faced nowadays. Yet upon the answer to this question depends the type of theory—integrative or analytic—which we adopt for explaining development and heredity. Aristotle saw this clearly, and dealt with the problem in a way which we must recognize to be masterly, and from which we can learn much. Aristotle had the great advantage over us of not being hindered in his biological thinking by the materialistic conceptions of later centuries, which, we may note incidentally, made havoc of his Physics. His whole philosophy is indeed a biological one.[1]

Let us consider how he dealt with the main pangenetic argument. 'First, then, the resemblance of children to parents is no proof that the semen comes from the whole body, because the resemblance is also found in voice, nails, hair, and way of moving, from which nothing comes. And men generate before they yet have certain characters such as a beard or grey hair' (722 a). There are two points to be noted specially here: (1) that no representative particle can come from dead products like nails or hair, and (2) that the resemblance lies essentially in functional activity. The latter is the important point. This is shown by a study of the following passage, which I quote here out of its turn in order to get at once into grips with Aristotle's meaning. 'For even if it were true', he writes, 'that it comes from all the *body*—as they say—they ought not to claim that it comes from all *parts* of it, but only from the creative part—from the workman, so to say, not from the material he works in. Instead of that, they talk as if one were to say that the semen comes from the shoes, for, generally speaking, if a son is like his

[1] See on this point 'Aristotle' by John Burnet, *Proc. British Academy*, xi, 1924.

father, the shoes he wears are like his father's shoes' (723 b). It is clear then that resemblance in nails and hair and shoes is a derivative resemblance, depending upon the more fundamental resemblance in manner of total functional activity.

Similarly the point that certain characteristics of maturity can be inherited from a youthful father is inexplicable on the pangenetic hypothesis, but understandable if the hereditary tendencies are inherited as a unitary whole.

Continuing the original argument, Aristotle writes: 'Further, children are like their more remote ancestors from whom nothing has come, for the resemblances recur at an interval of many generations. . . . The same thing applies also to plants, for it is clear that if this theory were true the seeds would come from all parts of the plants also; but often a plant does not possess one part, and another part may be removed, and a third grows afterwards' (722 a). These special difficulties of the theory of pangenesis have in modern times led to its replacement by the germ-plasm theory. It is, however, safe to say that Aristotle would not have accepted the theory of the germ-plasm without transforming it from a morphological into a functional theory. The next point considered by Aristotle is as to whether the semen is derived from the homogeneous parts (tissues) or from the heterogeneous parts (organs).[1] The passage must be quoted in full:

'We may also ask whether the semen comes from each of the homogeneous parts only, such as flesh and bone and sinew, or also from the heterogeneous such as face and hands. For if (1) from the former only, we object that the resemblance exists rather in the heterogeneous parts, such as face and hands and feet; if then it is not because of the semen coming from all parts that children resemble their parents in *these*, what is there to stop the homogeneous parts also from being alike for some other reason than this? If (2) the semen comes from the heterogeneous alone, then it does not come from all parts; but it is more fitting that it should come from the homogeneous parts, for they are prior to the heterogeneous which are composed of

[1] The distinction between homogeneous and heterogeneous parts corresponds in the main with our distinction of tissues and organs, but not completely; see my *Form and Function*, 1916, pp. 12–14.

them; and as children are born like their parents in face and hands, so they are, necessarily, in flesh and nails. If (3) the semen comes from both, what would be the manner of generation? For the heterogeneous parts are composed of the homogeneous, so that to come from the former would be to come from the latter and their composition.[1] To make this clearer by an illustration, take a written name; if anything came from the whole of it, it would be from each of the syllables, and if from these, from the letters and their composition. So that if really flesh and bones are composed of fire and the like elements, the semen would come rather from the elements than anything else, for how can it come from their composition? Yet without this composition there would be no resemblance. If again something creates this composition later, it would be *this* that would be the cause of the resemblance, not the coming of the semen from every part of the body' (722 a–b).

The argument is not too easy to follow, on account of Aristotle's condensed method of expression and the demands he makes on his reader,[2] so that some exposition is required. As to the first possibility, that the semen comes from the homogeneous parts alone, Aristotle objects that hereditary resemblance is essentially shown in the heterogeneous parts or organs; if then, *ex hypothesi*, resemblance in these parts can come about without the semen being derived from them, why should not the resemblance in the homogeneous parts also be due to this other cause? If (2) the semen comes from the heterogeneous parts only, and not from the homogeneous, we are up against difficulties, for we should naturally expect the semen to come from the constituents of the heterogeneous parts, that is, from the homogeneous parts. This difficulty is further discussed under (3), where it is pointed out that to come from the heterogeneous parts cannot only mean to come from the homogeneous parts and their 'composition', i.e. their arrangement and fitting together to form the heterogeneous parts. And, speaking in material terms, we cannot conceive of semen coming from this 'composition'. What is most likely is that the semen

[1] i.e. arrangement.

[2] What we possess of Aristotle are probably merely his lecture notes, not the works he prepared for publication; see Burnet, 1924.

comes from the primary elements of the homogeneous parts, which Aristotle called fire, water, and air. But hereditary resemblance is all in the mode of composition, in the way in which the elements are combined to form the tissues and in the arrangement of these to form the organs. No derivation of semen from any part can account for the re-constitution of this 'architectonic' resemblance. Hence the real cause of resemblance is the same factor that creates this organic architecture. Hereditary resemblance is, as it were, a by-product of development, and will be explained only when we succeed in explaining development.

The argument is clear and convincing, and is applicable *mutatis mutandis* to all modern theories that deal with representative particles, genes or the like.

After dealing with some other difficulties of the theory of pangenesis—how, for instance, the representative particles of the semen combine in the proper way to form the germ of a new organism, and how, if they are present in the generative secretions of both parents they combine to form one and not two 'little animals'—Aristotle comes back to his argument about the homogeneous and the heterogeneous parts and takes it a stage farther.

'Some parts', he writes, 'are distinguished by possessing a faculty, others by being in certain states or conditions; the heterogeneous, as tongue and hand, by the faculty of doing something, the homogeneous by hardness and softness and the other similar states. Blood, then, will not be blood, nor flesh flesh, in any and every state. It is clear, then, that that which comes from any part, as blood from blood and flesh from flesh, will not be identical with that part. But if it is something different from which the blood of the offspring comes, the coming of the semen from all the parts will not be the cause of the resemblance as is held by the supporters of this theory. For if blood is formed from something which is not blood, it is enough that the semen come from one part only, for why should not all the other parts of the offspring as well as blood be formed from one part of the parent. . . . Why not say that the semen from the very first is of such a kind that blood and flesh can be made out of it, instead of saying that it itself *is* blood and flesh?' (723 a).

Soon after comes the passage, already quoted, about the

semen and the shoes, which gives us the key to Aristotle's own view of development and heredity and lead us naturally to a discussion of his constructive theory. But before considering his conception of the cause and course of development let us examine the passage we have just quoted. It is notable for the definition of organ as distinguished by 'the faculty for doing something'. It further points out that the particles of the semen cannot have the same character as the parts from which they come—they must be 'germs' of these parts, such that from them the parts can be reconstituted. But it is clear that, if this is the case, the semen theory is quite useless as an explanation of development, for it already assumes development. If the semen-particle re-creates the part it represents, this is just as much a mystery as the development of the embryo as a whole—the problem is not disposed of by being split up in this way. This criticism also is fully applicable to all modern particulate theories of development and heredity.

The actual form of Aristotle's own theory of development has mainly historical interest at the present day. His knowledge of the essential facts was fragmentary, and he couched his explanation in terms of a philosophy to which we have nowadays some difficulty in attuning our minds. Nevertheless his fundamental idea, that development is the actualization of a functional potentiality, is a profound one and gets down to the root of the matter. We have seen that Aristotle rejected firmly the 'material' explanation offered by the theory of pangenesis, after demonstrating clearly its insufficiency. He deduced from his analysis of this theory that development is due to 'the creative part', or the creative power, which brings about the ordered 'composition' or putting-together of the tissues and organs to form the functional whole. This is the real cause both of development and of hereditary resemblance. He gave creative function the priority over structure; he held that the whole was greater than its parts.

His actual theory was that the female provided only the material for development, while the male provided the efficient and formal cause, the principle of putting together

or composition—as we should say, the formative impulse. The material possessed, at least potentially, the 'nutritive soul', rendering possible vegetative existence and sometimes growth; the male semen carried potentially the 'sensitive soul', which is the ground of movement and sense-perception, the distinguishing characters of the animal as compared with the plant. The semen derives its potentiality from the actuality of the male parent. Aristotle's line of thought in this connexion is rather difficult to follow, and for us it can only have the value of an analogy, derived from the consideration of human activity; it is fairly clearly put in the following passages. After speaking of 'automatic machines' in which an effect is produced by the linked action of one part upon another, he goes on:

'As, then, in these automatic machines the external force moves the parts in a certain sense (not by touching any part at the moment, but by having touched one previously), in like manner also that from which the semen comes, or in other words that which made the semen, sets up the movement in the embryo, and makes the parts of it by having first touched something though not continuing to touch it. In a way it is the innate motion that does this, as the act of building builds the house. Plainly, then, while there is something which makes the parts, this does not exist as a definite object, nor does it exist in the semen at the first as a complete part' (734 b).

Commenting upon the first part of this passage, Platt gives the following useful note: 'The male parent makes the semen and somehow imparts to it a potentiality of setting up movements in the embryo; this power given to the semen is like the impulse given to a piece of clock-work by pushing a wheel. Father=watchmaker, first wheel=semen, other wheels moved by the first=the parts developed by the semen.' He justly adds: 'We cannot solve the riddle any better at the present day; we can only say that no sooner has the spermatozoon penetrated the ovum than there is set up in the latter a series of movements which differentiate it and develop the parts one after another.' But let us continue the quotation:

'How is each part formed? We must answer this by starting in the first instance from the principle that, in all products of Nature or art,

a thing is made by something actually existing out of that which is potentially such as the finished product. Now the semen is of such a nature, and has in it such a principle of motion, that when the motion is ceasing[1] each of the parts comes into being, and that as a part having life or soul. For there is no such thing as face or flesh without life or soul in it; it is only equivocally that they will be called face or flesh if the life has gone out of them, just as if they had been made of stone or wood. And the homogeneous parts and the organic come into being together. And just as we should not say that an axe or other instrument or organ was made by the fire alone, so neither shall we say that foot or hand were made by heat alone. The same also applies to flesh, for this too has a function. While, then, we may allow that hardness and softness, stickiness and brittleness, and whatever other qualities are found in the parts that have life and soul, may be caused by mere heat and cold, yet, when we come to the principle (λόγος) in virtue of which flesh is flesh and bone is bone, that is no longer so; what makes them is the movement set up by the male parent, who is in actuality what that out of which the offspring is made is in potentiality. This is what we find in the products of art; heat and cold may make the iron soft and hard, but what makes a sword is the movement of the tools employed, this movement containing the principle of the art. For the art is the starting-point and form of the product; only it exists in something else, whereas the movement of Nature exists in the product itself, issuing from another nature which has the form in actuality' (734 b–735 a).

The semen is not even a necessary link in the chain, for:

'The male does not emit semen at all in some animals, and where he does this is no part of the resulting embryo; just so no material part comes from the carpenter to the material, i.e. the wood in which he works, nor does any part of the carpenter's art exist within what he makes, but the shape and the form are imparted from him to the material by means of the motion he sets up. It is his hands that move his tools, his tools that move the material; it is his knowledge of his art, and his soul, in which is the form, that move his hands or any other part of him with a motion of some definite kind, a motion varying with the varying nature of the object made. In like manner, in the male of those animals which emit semen, Nature uses the semen as a tool and as possessing motion in actuality, just as tools are used in the products of any art, for in them lies in a certain sense the motion of

[1] The text is doubtful here.

the art. Such, then, is the way in which these males contribute to generation. But when the male does not emit semen, but the female inserts some part of herself into the male,[1] this is parallel to a case in which a man should carry the material to the workmen. For by reason of weakness in such males Nature is not able to do anything by any secondary means, but the movements imparted to the material are scarcely strong enough when Nature herself watches over them. Thus here she resembles a modeller in clay rather than a carpenter, for she does not touch the work she is forming by means of tools, but, as it were, with her own hands' (730 b).

The passage in which Aristotle points out that 'there is no such thing as face or flesh without life or soul in it' is cardinal to an understanding of his view. It is important to realize that this view was not 'vitalistic' in the modern sense of implying a dualism of matter and 'entelechy'; for Aristotle 'soul' in this connexion was an expression for the total functional activity of the organic unit or part considered—its activity *as a whole*. This is certainly true of the 'nutritive' and the 'sensitive' soul, but must be qualified for the 'rational' soul, to which is attributed a certain independence of the body, 'for no bodily activity has any connexion with the activity of reason' (736 b). The other two kinds are dependent on the body for their manifestation, for 'those principles whose activity is bodily cannot exist without a body, e.g. walking cannot exist without feet' (736 b). Both the semen and the unfertilized egg have the nutritive soul potentially but not actually; the semen has in addition the sensitive soul potentially, but this soul cannot become actual or active until the embryo develops, and the organs of perception and movement are formed.

Abstracting from the particular form of Aristotle's theory and stating only the essential core, we may say that he regarded what we should now call the fertilized ovum as possessing potentially the functional capabilities of the parents, and development as being the actualization of these potentialities. The major part of them come from the male parent, for the female contributes only material, containing

[1] As Aristotle thought was the case in certain insects. Cf. 721 a.

potentially the nutritive soul. Soul=functional activity, and exists in the fertilized ovum in a potential state. Resemblance between parents and offspring is a consequence of their starting out with the same developmental potentialities; it cannot be explained as a point-to-point or particulate inheritance due to the transference of material particles. The physical properties of the homogeneous parts, and of their constituent elements, come in only as conditioning development, not as causing it. We shall see later, in Chapter X, that this conception is still of fundamental importance. Material properties, such as heat and cold, could not in Aristotle's opinion account for development. Growth was due to the power of the nutritive soul, 'using heat and cold as its tools in accordance with a principle' (740 b).

Some properties of the tissues of the developing organism are due to 'necessity'—as we should say, 'material causes'—but above all this there is the final and efficient cause in which the real explanation lies (743).

I said above that Aristotle would not have accepted any germ-plasm theory in its modern structural form. But there is a certain analogy between his explanation of hereditary resemblance as due to identity of developmental potentialities, and the modern explanation in terms of identity of germinal constitution—the one theory deals in functions actual and potential, the other in structures; and the structural germinal complexities which modern theory finds it necessary to postulate are merely the translation into material terms of Aristotle's functional potentialities. In a sense one explanation is as good as the other, but Aristotle's has the merit of being simpler and not requiring any elaborate hypothetical machinery.

Aristotle was, of course, an out-and-out believer in epigenesis. He based his opinion partly on observation and partly on reasoning. His theory made it unnecessary to assume that any part existed ready-made either in the semen or in the material supplied by the female. He puts the alternatives of preformation or epigenesis as follows:

'Either all the parts, as heart, lung, liver, eye, and all the rest, come

into being together or in succession, as is said in the verse ascribed to Orpheus, for there he says that an animal comes into being in the same way as the knitting of a net. That the former is not the fact is plain even to the senses, for some of the parts are clearly visible as already existing in the embryo while others are not; that it is not because of their being too small that they are not visible is clear, for the lung is of greater size than the heart, and yet appears later than the heart in the original development' (734 a).

He raises too the question as to whether the succession of parts is a causal or a temporal succession and concludes that it is merely temporal. His reason is that 'in all the productions of Nature or of art, what already exists potentially is brought into being only by what exists actually; therefore if one organ formed another the form and the character of the later organ would have to exist in the earlier, e.g. the form of the liver in the heart'—which is absurd (734 a).

The point is further discussed in a later chapter. After comparing the embryo with the seeds of plants he goes on: 'So also in the embryo all the parts exist potentially in a way at the same time, but the first principle is furthest on the road to realization. Therefore the heart is first differentiated in actuality. This is clear not only to the senses (for it is so) but also on theoretical grounds' (740 a).

And summing up, he writes: 'Now the parts of the embryo already exist potentially in the material, and so when once the principle of movement has been imparted to them they develop in a chain one after another, as the wheels are moved one by another in the automatic machines' (741 b). This is not of course to be understood in the modern sense that one stage of ontogeny is the cause of the next, but rather that the 'movement' imparted by the semen is the primary and underlying cause of the whole process.

Development, Aristotle noticed, was from the general to the special. The unfertilized embryo, before receiving the activating impulse from the semen, is possessed of the nutritive soul and lives the life of a plant. As it develops after 'fertilization' by the semen, the embryo acquires the sensitive soul in virtue of which an animal is an animal. Furthermore,

'an animal does not become at the same time an animal and a man or a horse or any other particular animal. For the end is developed last, and the peculiar character of the species is the end of the generation in each individual' (736 b). We have here a clear foreshadowing of K. E. von Baer's law of development.

There is an indication, too, of the truth, emphasized many centuries later by W. Roux, that many organs are formed in advance of functioning. Thus, 'those which breathe and whose parts are differentiated within the mother's uterus yet do not breathe until the lung is perfected, and the lung and the preceding parts are differentiated before they breathe. Moreover, all polydactylous quadrupeds, as dog, lion, wolf, fox, jackal, produce their young blind, and the eyelids do not separate till after birth' (742 a).

There are many other points of interest in Aristotle's treatise on which much time might be spent. We shall mention only one or two. His ideas on sex were necessarily crude, but he did point out that separate sexes were characteristic of animals that move, whereas sedentary animals, like plants, had no sex (715) or as he explains later (731 a) were male and female combined. 'In all animals which can move about, the sexes are separated, one individual being male and one female. . . . But in plants these powers are mingled, female not being separated from male. Wherefore they generate out of themselves, and do not emit semen but produce an embryo, what is called the seed' (731 a). There follows the quaint suggestion that animals 'seem literally to be like divided plants, as though one should separate and divide them, when they bear seed, into the male and female existing in them'. The rationale of the separation of the sexes in motile animals is to enable them to develop the faculties of the sensitive soul. 'For to the essence of plants belongs no other function or business than the production of seed; since, then, this is brought about by the union of male and female, Nature has mixed these and set them together in plants, so that the sexes are not divided in them. . . . But the function of the animal is not only to generate (which

is common to all living things), but they all of them participate also in a kind of knowledge, some more and some less, and some very little indeed. For they have sense-perception, and this is a kind of knowledge' (731 a). Such knowledge may be very inferior as compared with intellect, but it is 'most excellent' as compared with the absolute insensibility of the inorganic world. For Aristotle there were of course four grades of existence—matter, vegetative existence, the life of sense perception, and the life of reason. In man all are combined in a hierarchy; in animals the first three, and in plants two only.

The problem of sex-determination had great interest for Aristotle; he discussed all the current views and worked out a new solution of his own, which we need not however consider here.

We have seen that Aristotle realized the important point that the explanation of hereditary resemblance is dependent upon the explanation of development, that this resemblance is a feature of development rather than a separate problem. It is of interest to reproduce here his summary of the facts of heredity, which shows that he had gone very carefully into the matter.

'(1) Some children resemble their parents, while others do not, some being like the father and others like the mother, both in the body as a whole and in each part, male and female offspring resembling father and mother respectively rather than the other way about. (2) They resemble their parents more than remoter ancestors, and resemble those ancestors more than any chance individual. (3) Some, though resembling none of their relations, yet do at any rate resemble a human being, but others are not even like a human being but a monstrosity' (767 b).

The second generalization has quite a biometric turn, and only wants precise formulation to give us Galton's law.

In concluding this slight sketch of Aristotle's views on heredity and development I should like to emphasize the fact that the *De Generatione Animalium* is a veritable mine of philosophic thought and well worth a much more thorough investigation than has been attempted here. I have merely detached the main ideas which seem to have permanent significance for any and every theory of development and heredity.

III

PREFORMATION AND EPIGENESIS

IN the long stretch of time from Aristotle to the nineteenth century there is little to interest us from the purely theoretical point of view save the origin and growth of the preformistic theories of development. Historically the later centuries are important, and if it were our intention to trace out the evolution of *knowledge* about heredity and development it would be necessary to treat them in full detail. We are not, however, primarily concerned with the history of discovery, but rather with those fundamental conceptions which are ageless and persist, however much they may be altered, extended, or transformed by the discovery of new facts. We are far from wishing to minimize the importance of the discovery of facts, of that vast extension of knowledge which is the essential achievement of nineteenth- and twentieth-century science. It is indeed solely due to this patient and long-continued investigation that an understanding of the essential facts about reproduction and development at last became possible about the middle years of the nineteenth century. Until the facts of organic continuity became manifest, until the egg and the spermatozoon were recognized to be cells, until the behaviour of the chromosomes in maturation and fertilization was discovered, the basis for the modern ideas about development and heredity simply did not exist. And all this did not become fully established till about the 'seventies. We are justified therefore in passing very lightly over all theories prior to the modern, paying attention only to those fundamental ideas which, being as it seems rooted in the constitution of the human mind, are ever alive and active even in the most modern and apparently novel theories.

In the main, Aristotle's conception of development remained dominant right down to the seventeenth century. William Harvey, following up the embryological researches of his teacher Fabricius, departed not at all in his theoretical

views from the doctrine of Aristotle.[1] He had no conception of genetic continuity; the famous dictum *Omne vivum ex ovo*, which is ascribed to him but does not occur in this form in his writings, did not mean that all living things were developed from ova as we understand the word, and it was perfectly consistent with the belief in spontaneous generation which Harvey shared with Aristotle. The term ovum for Harvey meant the undifferentiated embryo, and covered also the larva and pupa of insects.

Harvey was, of course, like Aristotle, an upholder of epigenesis, or the gradual and successive differentiation of the germ. The opposing doctrine of preformation arose almost in Harvey's lifetime, and was first stated by Malpighi. It is difficult to allot any one cause for the appearance of this new doctrine; it seems, however, certain that one important contributory factor was the establishment in the seventeenth century of the mechanistic view of the universe as a result of the astronomical and physical researches of Kepler, Galileo, and Newton, and the philosophical criticism of Descartes. This view was directly opposed to Aristotle's 'biological' theory of the universe, and led to an entirely new conception of the nature of living things. These came to be regarded as machine-like, as soulless automata whose actions were a mechanical consequence of their structure. At the same time the introduction of the microscope revealed the structural complexity of the lower animals, and what the eye could not see through the imperfection of the instrument the mind readily imagined.

This point is well treated by Wheeler.[2]

'The microscope,' he writes, 'invented in the sixteenth and bequeathed to the seventeenth century, had profoundly influenced speculation. Magnification had revealed, as if by magic, the existence of a great world of structures undreamed of by the greatest intellects the race had hitherto produced. . . . The mind, full of the great

[1] See E. Rádl, *Geschichte der biologischen Theorien in der Neuzeit*, i, 2nd Ed., Leipzig and Berlin, 1913, pp. 134–9. Also C. O. Whitman, 'Evolution and Epigenesis' in *Wood's Holl Biological Lectures for 1894*, Boston, 1895, pp. 216–19.

[2] W. M. Wheeler, 'Caspar Friedrich Wolff and the *Theoria Generationis*', *Wood's Holl Biological Lectures for 1898*, Boston, 1899.

microscopic discoveries of the time, was carried away by its own inertia, and, outrunning the instrument, first dreamed of and then believed in the existence of structures too minute to be revealed by the available lenses. . . . It was natural but erroneous to conceive unseen structures as diminutive duplicates of the seen. The verisimilitude of this error increased when it became apparent that the microscope was unable to resolve perfectly transparent structures even of considerable size' (p. 270).

It was natural then to assume in the germ a complicated machine-structure corresponding with the visible structure of the adult.

The belief in spontaneous generation was also gradually overcome in this country. Redi's experiments showed that insects did not arise from decaying matter, as the ancients had believed, but by processes of sexual reproduction as in the higher animals. The idea of organic continuity—*Omne vivum e vivo*—therefore made headway, at the expense of the older Aristotelian view, and to the advantage of the preformationists.

Another factor which undoubtedly helped in the establishment of the preformationist view was the Biblical doctrine of creation. The early mechanistic view was easily reconcileable with the belief in a Divine Creator, who made the world-machine once for all and set it going, thereafter resting from His labours. The world and all the creatures therein were on this view called into existence by the creative Fiat, and all that happened subsequently was predestined and predetermined—the movements of the celestial spheres, all history, all development. No new creation ever took place. Hence also in the development of the living thing there could be no new formation; the essential structure was there from the beginning, and development merely an unfolding. Preformation was essentially a derivative of the philosophical doctrine of determinism; whether this original predetermination was due to a Divine act of creation or to 'blind chance' (as in the materialistic view) amounted to very much the same thing.

Wheeler, in the excellent paper already referred to, traces

the preformationist view to the 'Platonizing' tendency of the human mind. All thinkers, he considers, from the earliest times fall into one or other of two classes. The first are impressed by the flux of things, the succession of events. Theirs is the philosophy of change and their high priest is Heraclitus. The other group fasten on the recurrence of similar forms, the identities underlying change. Theirs is the philosophy of rest and fixity, and they go back to Parmenides.

'The contrast in these two views reappears between Aristotle and Plato. This difference is seen in the all-pervading movement as conceived by Aristotle in his Physics, in contrast with the "ideas" of Plato.... Plato, under the influence of Parmenides and the philosophy of rest, emphasizes the forms and qualities that keep recurring to our minds in time and space, generalizing them into his "ideas" and endowing them with all the attributes of reality' (p. 266).

This difference between the two types of mind comes out very clearly in the study of development:

'Under the influence of the Christian church the Platonic conception seems to have led to the notion of the special creation of fixed types or forms. It culminated in that finished theory of predelineation in embryonic development known as *emboîtement*. This was, in reality, the very negation of all development, since the theory held that all the individuals of a species had been created simultaneously for all time' (pp. 267–8).

Even at the present day, Wheeler points out, the difference of attitude shows itself in our theories of development.

'He who finds little difficulty in passing from the simple to the complex, from the homogeneous to the heterogeneous, will take an epigenetic view of development. The physiologist, who deals with processes, who is ever mindful of the Heraclitean flux, inclines naturally to this view. On the other hand, he who readily idealizes and schematizes, whose mind is endowed with a certain artistic keenness, an appetite for forms and structures, and a tendency to make these forms final patterns, eternal moulds, more permanent than the substance that is poured into them—such a one will find more difficulty in understanding *how* the homogeneous can become the heterogeneous. Of this type is the modern morphologist who is continually diagrammatizing, who has his eye fixed on complex static

structures and conceives the continually changing form of the developing egg as a series of kinematograph pictures in three dimensions of space. He is as much inclined to Platonize as is the modern physiologist to reason along lines suggested by Aristotle. He is by nature a preformationist' (p. 282).

That is an acute and profound analysis, and gets very near the essential truth. Epigenesis and preformation represent two different attitudes to the problem of development, arise from two fundamentally different philosophies. The epigenetic view is dynamic, vitalistic, physiological; the preformationist is static, deterministic, and morphological. The one stresses time or process, the other space and momentary state—the one emphasizes function, the other concentrates on form.

The preformistic theories, in the actual form which they took in the seventeenth and early eighteenth centuries, are of little importance or interest in relation to modern views of development and heredity. It is unnecessary for us to consider them in detail; the fascinations of the doctrines of *emboîtement* shall not tempt us, nor the battles of the ovists and spermatists.[1]

The preformationists contributed nothing of value to the understanding of our problems. Whitman sums the position up very neatly when he says:[2] 'Evolution [preformation] was the absolute negation of both heredity and generation, while epigenesis upheld generation, but denied organic continuity, the essential foundation of heredity' (p. 226). What is chiefly of interest to us is the general attitude of mind that produced the preformistic theories.

One of the later preformationists, however, Charles Bonnet, who belongs to the middle and later years of the eighteenth century, merits rather fuller treatment, since he was the first originator of certain ideas which play a great part in some later theories, notably Weismann's. I refer particularly to the notion of determinants.

[1] On which see R. C. Punnett, 'Ovists and Animalculists', *American Naturalist*, lxii, 1928, pp. 481–507.

[2] 'Bonnet's Theory of Evolution', *Wood's Holl Biological Lectures for 1894*, Boston, 1895.

Bonnet's views have been discussed in a very adequate way by Whitman,[1] whom we shall follow in our treatment of the subject.

While some of the earlier preformationists thought of the germ as an adult in miniature, and imaginative souls saw in the spermatozoon a tiny homunculus with head and arms and feet, Bonnet makes it clear that while all the parts are represented in the germ, they have not necessarily the same form, arrangement, and appearance as in the adult. 'Tandis que le poulet est encore dans l'état de germe, toutes ses parties ont des formes, des proportions, des situations qui diffèrent extrêmement de celles que l'évolution leur fera revêtir. Cela va au point, que si nous pouvions voir ce germe en grand, tel qu'il est en petit, il nous serait impossible de la reconnaître pour un poulet' (quoted by Whitman, p. 235, f.n.). The organs pre-exist as 'organic points' forming, as it were, the nucleus of future organization.

'The principal difference', he writes, 'between the germ and the developed animal is that the first is composed of *elementary particles* alone, and that the meshes which they form are as narrow as possible; while, in the second, the elementary particles are joined to an infinite number of other particles which nutrition has associated with them, and the meshes of the simple fibres are enlarged as much as the nature and the arrangement of their principles will admit' (Whitman, p. 245).

The following passages translated by Whitman from his 'Palingénésie philosophique' (1769) give a good idea of Bonnet's position.

'I first assumed, as a fundamental principle, that nothing was generated; that everything was originally preformed, and that what we call generation was but the simple development of what pre-existed under an invisible form and more or less different from that which becomes manifest to our senses.

'I postulated that all organized bodies derived their origin from a germ which contained *très en petit* the elements of all the organic parts.

[1] Paper above mentioned, and 'The Palingenesia and the Germ Doctrine of Bonnet,' in same volume, pp. 241–72.

'I conceived the elements of the germ as the primordial foundation, on which the nutritive molecules went to work to increase in every direction the dimensions of the parts. . . . The primitive organization of the germs determines the arrangement which the nourishing atoms must take in order to become parts of the organic whole. . . . I considered the organic whole, attained to its full growth, as a composite of original or elementary parts and of foreign substances which nutrition had associated with them during the entire course of life' (Whitman, pp. 246–7).

What was preformed was not the organs in miniature, but organic particles corresponding to *and determining the growth of* the organs. The analogy with the 'seeds' of Hippocrates (the 'semen' coming from all the parts[1]) and the determinants of Weismann[2] is unmistakable; nor can we miss the obvious foreshadowing of the distinction drawn by Nägeli between idioplasm and trophoplasm (see below, p. 42).

Bonnet conceived these representative particles to be as a rule combined into complete germs (like Weismann's *ids*), but the study of regeneration in *Hydra* and other forms led him to admit that they might also exist separately or in groups, forming thus germs of parts (Whitman, pp. 266–71). The explanation of regeneration, as due to germs held in reserve (previously suggested by Réaumur), is clearly the same in principle as that put forward by Weismann at a much later date. Bonnet's views indeed bridge over the gap between the old preformation doctrine and its modern equivalent.

One further remark about Bonnet. It appears from an interesting passage quoted by Whitman that one of his main reasons for accepting the theory of preformation was that epigenetic development appeared to him to be inexplicable on mechanical grounds. 'If organized bodies are not preformed, then they must be formed every day, in virtue of the laws of a special mechanics. Now, I beg you to tell me what mechanics will preside over the formation of a brain, a heart, a lung, and so many other organs?' He goes on to elaborate

[1] As 'germs' of these parts, cf. Aristotle, p. 17 above.
[2] See p. 43 below.

this difficulty, adducing the complexity, co-ordination, and harmony of structure which characterize the higher animals —and even the lower animals also, as Lyonet had recently shown for the goat-moth caterpillar.

'I only ask one favour of those who are fond of mechanical explanations; that is, that they will cast a glance at the wonders produced by the graver of the celebrated Lyonet. They will not behold without profound astonishment those four thousand muscles employed in the construction of a caterpillar, their admirable co-ordination, and that of the tracheae, which is no less admirable. And I am fain to persuade myself they will then feel that a whole so marvellously composed and yet so harmonious, so essentially one, cannot have been formed, like a watch, of related pieces, or by the ingraining of an infinitude of diverse molecules united by successive opposition. They will admit, I hope, that such a whole bears the indelible imprint of a work done at a single stroke. . . . I limit myself to saying that, in the actual state of our knowledge of the physical world, we do not discover any rational way of explaining mechanically the formation of an animal, or even the least organ. I therefore think it more consonant with sound philosophy, because it is more consonant with facts, to admit, as at least highly probable, that organized bodies pre-existed from the beginning' (Whitman, p. 259).

The difficulty of accounting for differentiation, the production of new form, on mechanistic principles, has driven many to deny like Bonnet the reality of development, as the only way of escaping the non-mechanical theory of epigenesis. But it is only the convinced mechanist who finds it necessary so to take refuge in the comfortable doctrine of preformation. Those who do not accept the mechanistic scheme are under no such compulsion. Here then is another proof of the close relation which exists between materialism and the preformistic theory.

With Bonnet the doctrine of preformation reached its fullest development, ripened, and fell. During his lifetime the way back to the Aristotelian doctrine of epigenesis was pointed out by C. F. Wolff, whose thesis, *Theoria generationis* (1759), published when he was only twenty-six, is justly regarded as one of the classical writings on embryology. Wolff avoided the facile speculations about development

which were popular in his day; he built up his views on a sound basis of painstaking observation, following out the development of the chick with as great accuracy as his instruments permitted, and thinking clearly and logically about what he saw. His actual theory of development is of little practical interest now; it relied upon the interaction of two forces, the *Vis essentialis*, which was frankly vitalistic, and the 'coagulative power' (*Solidescibilitas*).[1] He made a bold attempt to explain the development both of plants and of animals by means of these two principles. It is difficult for us nowadays to grasp what Wolff really meant; one gets the impression in reading him that he was striving towards a physiological theory of development, but never quite getting there, on account of the almost complete lack of real physiological knowledge in his time. He is constantly trying to connect up assimilation, growth, and differentiation. Though he refers to the theory of 'predelineation' only here and there, his whole book is an attack upon the preformistic theory. He refutes it on the ground of simple observation. When we examine a very early chick embryo we find that 'It consists of a mass, characterized only by its external form and condition, and for the rest composed of globules showing little coherence and simply heaped together; it is transparent, capable of movement, and almost liquid, and shows no trace of heart or vessels, nor of red blood'.[2] He goes on: 'In general we cannot say that what cannot be perceived by the senses does not therefore exist. This principle is more subtle than true when applied to these observations. The particles which constitute all animal organs in their earliest beginnings are little globules, which may always be distinguished under a microscope of moderate magnification. How, then, can it be maintained that a body is invisible because it is too small, when the *parts* of which it is composed are easily distinguishable?' When we magnify the chick blastoderm we do not

[1] An account of the theory is given by Rádl, pp. 244–7, and by Wheeler, op. cit., pp. 273 ff.

[2] *Theoria generationis*, para. 166 (p. 3 of Part II in edition published in Ostwald's *Klassiker der exakten Wissenschaften*, Leipzig, 1896).

bring into view a miniature of the adult; the microscope reveals a totally different picture—an assemblage of globules or cells which bear no resemblance to the parts of the future embryo.

Wolff was constitutionally a vitalist of the Aristotelian stamp; he emphasized always the driving force behind development, and regarded form as subsidiary to function. Goethe, who links up with Wolff in an interesting way through his theory of the metamorphosis of plants, also expressed belief in a formative force or *Bildungstrieb*, which works out the 'idea' of the organism.[1]

By the early days of the nineteenth century the theory of preformation had sunk to the level of a popular belief, and in his masterwork on development[2] K. E. von Baer pays little attention to it. In refuting it he takes the same line as C. F. Wolff—the direct appeal to observation. His comments on the mentality of its upholders are interesting and deserve quotation. 'It will ever be found', he writes, 'that, of all possible courses we can imagine, Nature chooses the simplest and most obvious.... But our fantasy so easily oversteps the simple way of Nature!' (i, p. ix). Or again, with more direct reference to the theory of *emboîtement*—'Although this hypothesis borders on the insane, it has been advocated by very distinguished naturalists, and it affords a striking example of the aberrations into which one can fall if we systematically follow assumption rather than observation.... But Nature gives her observer cause only for admiration at the simplicity with which she works, and for astonishment at the proneness of the human wit to explain any phenomenon which appears remarkable, by means of infinitely greater and more incomprehensible wonders' (ii, pp. 6–7).

Baer was the founder of modern embryology, and his book was the finest work of its kind since Aristotle. Its main interest is perhaps morphological,[3] but we can glean from it

[1] See *Form and Function*, 1916, pp. 50–1.

[2] *Ueber Entwickelungsgeschichte der Thiere, Beobachtung und Reflexion*, Königsberg, i, 1828, and ii, 1837.

[3] I have dealt with this aspect in *Form and Function*, 1916, chap. IX.

a clear idea of Baer's views on the nature of development. Baer was not a materialist. He considered that development could not be fully explained as a succession of stages causally related to one another; there was something more involved, namely the 'Wesenheit', the essential nature, of the animal. It is necessary to quote his own words to make this point clear—'Although it is self evident that, while each step in development is only rendered possible by the preceding state, the whole course of development is nevertheless ruled and guided by the essential nature of the future organism, and that any one state is not the sole and absolute conditioning factor of the future, it is not without interest to be able to demonstrate these facts by observation' (i, p. 147). Baer goes on to illustrate this by showing that the large variations which may occur in early embryonic life are smoothed out by a process of regulation as development proceeds. Whereas nowadays it is widely believed, under the influence of the materialistic conception, that each stage of development is the sufficient cause of the next following stage, Baer held that one stage, while it *conditioned* the next, was not in any full sense its cause. The real cause was, in his view, the future and final form to which development converged. As against the materialist explanation he maintained that 'it is not the *matter*, in its mere arrangement, but the *essential nature* (the Idea according to the new school) *of the procreating organism* that rules the development of the offspring' (i, p. 148). A vitalistic and teleological point of view, no doubt, but containing, as we shall see later, a truth essential to the proper understanding of development. The analogy is striking with Aristotle's view that development is not explicable in terms of material properties such as 'heat' and 'cold', but must be regarded as due to the 'actuality' of the procreating male imposing a certain course of development upon the formless germinal material.

The main characteristics of development were, in Baer's view, first, the increasing autonomy and independence of the developing organism, and second, the fact that development is essentially a process of differentiation proceeding from the

general to the special. He distinguished three processes of differentiation in the early stages, namely, 'primary differentiation' or the formation of germ-layers, 'histological differentiation', and the 'morphological differentiation' of the elementary organs. The fact that development proceeds from the general to the special he used to refute the crude form of the recapitulation theory which was current in his day, summarizing his conclusions in the following laws:

'(1) That the general characters of the large group to which the embryo belongs appear in development earlier than the special characters. . . .

(2) From the more general structural relations the less general develop, and this process continues till the most specialized appear.

(3) The embryo of any given form, instead of recapitulating other definite forms, on the contrary separates itself from them.

(4) Fundamentally the embryo of a higher animal never resembles the adult of another animal, but only its embryo' (i, p. 224).

The five 'Scholia' in which Baer states and discusses the main deductions to be drawn from his description of the development of the chick, some of which we have considered briefly above, merit fuller treatment than can be given here. We shall content ourselves with quoting his own final summing up:

'If we consider the purport of the Scholia as a whole, a general conclusion can be drawn therefrom. We found that the effect of procreation lies in this, that the part is raised to the rank of a whole; during development independence grows in relation to environment, just as the form becomes more definite; in the evolution of internal structure, more specialized parts grow out from the general parts and their differentiation increases; the individual as the bearer of a definite organic form gradually passes from the general to the more special, so that the general conclusion from these investigations and observations can thus be expressed:

The history of the development of the individual is the history of the growing individuality in all its relations' (i, p. 213).

Reproduction is essentially the formation of a new individuality, a new whole; the ovarian egg is under the control of the parent organism; through fertilization a whole

develops from this which was originally a part (i, p. 150). Development is essentially a process of differentiation, accompanied by an increase in the independence and autonomy of the developing organism over against its environment—in sum, a growth of individuality or wholeness. We have seen above that Baer recognized also the importance of regulatory processes.

Baer's philosophical standpoint is definitely anti-materialistic. He is clearly influenced by Kant's teleology, but appears to go farther in the direction of a sort of universal vitalism. He refers in the second volume of his great work to the attempts being made in his own time to explain life in physico-chemical terms, and remarks that such attempts must always remain incomplete and unsatisfactory, since life can be explained only in terms of itself. The passage may be quoted:

'But all explanations of this [materialistic] kind the physiologist finds soon to be highly incomplete, since they touch only one single side of life; and he comes to see, above everything, that life cannot be explained from something else, but must be conceived and understood in itself. The time is approaching when even the physicist must admit that in his investigations he merely puts together the isolated physical antecedents of the totality of life, and thereby fashions for himself an artificial beginning' (ii, p. 3).

His vitalistic and teleological tendency is strongly expressed in certain of the essays republished in his Lectures.[1] Thus in an essay (dating from 1834) on 'Nature's most general law in development and evolution', after discussing the evidence for evolution and considering the facts of development, he concludes that the ultimate law of all creative processes is 'the progressive victory of spirit over matter' (*Reden*, i, p. 71). In another essay in the same volume the following remarkable passage occurs: 'Therefore instinct seems to me to be the completion of the life-process. We do not regard the life-process as a result of its organic constitution but as the rhythm, almost the melody, according to which the organic body builds and rebuilds

[1] *Reden*, St. Petersburg, i, 1864; ii, 1876.

itself. Naturally the means must be found in the organism by which the individual functions of the life-process can express themselves. But from these the life-process does not come, otherwise they would have no unity' [1] (*Reden*, i, p. 280).

What attitude Baer adopted towards the dualism which almost inevitably attaches to a vitalistic conception of living things is not quite clear. He was almost more a poet than a philosopher. There is a definite hint however, in the following passage, that the rigid distinction generally made between matter and spirit might be due to the limitations of the human intellect, and that this dualism could be overcome. 'Is it not owing to our intellectual limitations that we are compelled to regard the past, present, and future as always separated, that we can form no clear idea of an existence without a beginning and conditioning causes, because we must be always demanding such causes, and that we treat force and matter, spirit and body as separate in their essence, although they are spatially united?' (*Reden*, ii, pp. 79–80). Truly a penetrating and prophetic passage!

[1] Cf. Aristotle, p. 17 above.

IV

THE GERM-PLASM THEORY

IN the charming preface to his *Vorträge über Descendenz-theorie* (1902) Weismann remarks that a theory to be really valuable and stimulating should be clear cut and definite, so that if it be faulty it can be amended and if false rejected. The remark applies with special force to his own theory of the germ-plasm, which, though later shown to be incorrect in many respects, exercised through its precise and clear formulation a great and lasting influence on biological thought.

Weismann summed up in his theory many ideas which were just becoming ripe for expression, and he owed much to Darwin, Galton, Nägeli, and H. de Vries; it is convenient to take his theory as typical of a method of thought which even at the present day retains a considerable measure of vitality.

The development of the cell-theory had by the 'fifties and 'sixties of the nineteenth century led to a clear conception of cellular continuity; it was known that both the ovum and the spermatozoon were single cells, and it was held that all development took place by means of division and growth of cells. The way was thus open for an explanation of heredity in terms of the transmission from germ-cell to germ-cell of the essential potentialities of development. A direct unchanged continuity between the germ-cells of one generation and the germ-cells of the next could, however, be demonstrated only in rare cases; and his theory of heredity was from the beginning stated by Weismann in terms of germinal *substance*, not in terms of germinal cells. In his essay of 1883, 'Ueber die Vererbung', after pointing out that the germ-cells become differentiated at very varying periods in the life-history of the different groups, he goes on: 'Thus, as their development shows, a marked antithesis exists between the substance of the undying reproductive cells and that of the perishable body-cells. We cannot explain

this fact except by the supposition that each reproductive cell potentially contains two kinds of substance, which at a variable time after the commencement of embryonic development, separate from one another, and finally produce two sharply contrasted groups of cells.'[1]

In this essay the essential lines of the germ-plasm theory are laid down, though in general terms, and the point is emphasized 'that the understanding of the phenomena of heredity is only possible on the fundamental supposition of the continuity of the germ-plasm' (ibid., p. 106).[2]

It is, however, in the paper of 1885, 'Die Kontinuität des Keimplasmas', that we find the clearest summary of the basic principles of his theory. Here he writes, after criticizing and rejecting Darwin's theory of pangenesis, that there remain

'only two other possible, physiologically conceivable, theories as to the origin of germ-cells, manifesting such powers as we know they possess. Either the substance of the parent germ-cell is capable of undergoing a series of changes which, after the building-up of a new individual, leads back again to identical germ-cells; or the germ-cells are not derived at all, as far as their essential and characteristic substance is concerned, from the body of the individual, but they are derived directly from the parent germ-cell.

'I believe that the latter view is the true one. . . . I propose to call it the theory of "The Continuity of the Germ-plasm", for it is founded upon the idea that heredity is brought about by the transference from one generation to another, of a substance with a definite chemical, and above all, molecular constitution. I have called this substance "germ-plasm", and have assumed that it possesses a highly complex structure, conferring upon it the power of developing into a complex organism. I have attempted to explain heredity by supposing that in each ontogeny, a part of the specific germ-plasm is not used up in the construction of the body of the offspring, but is reserved unchanged for the formation of the germ-cells of the following generation.

'It is clear that this view of the origin of germ-cells explains the

[1] A. Weismann, *Essays upon Heredity*, Eng. Trans., 2nd ed., vol. i, Oxford, 1891, p. 74.

[2] The fundamental idea of the continuity of germinal substance had already been expressed by Galton (1875), Jaeger (1876), and Nussbaum (1880).

phenomena of heredity very simply, inasmuch as heredity becomes thus a question of growth and assimilation, the most fundamental of all vital phenomena. If the germ-cells of successive generations are directly continuous, and thus only form, as it were, different parts of the same substance, it follows that these cells must, or at any rate may, possess the same molecular constitution, and that they would therefore pass through exactly the same stages under certain conditions of development, and would form the same final product. The hypothesis of the continuity of the germ-plasm gives an identical starting-point to each successive generation, and thus explains how it is that an identical product arises from all of them' (ibid., p. 170).

There are two fundamental points to note in this confession of faith; first, that heredity is due to the transmission from one generation to another of a peculiar substance of complex molecular structure, which though subject to metabolism remains essentially unchanged; second, that this substance exercises a direct, determining, influence upon development. The fact that development takes the same course in successive generations is explained quite simply by the supposition that its starting-point is always the same. The environment of the developing organism is assumed to be constant and is thereafter left out of the picture.

In the essay of 1883 the germ-plasm is not identified with any particular constituent of the cell; it is treated as a hypothetical substance whose existence logic forces us to postulate. In 1885, however, Weismann identifies it with the nuclear substance of the germ-cells. The brilliant cytological work of O. Hertwig, E. Strasburger, E. van Beneden, and others, which was bearing fruit about this time, showed clearly that the essential thing in normal fertilization was the union of the maternal and paternal nuclei. Pflüger's discovery of the apparent isotropism of the frog's egg seemed to indicate that the cytoplasm took no part in the transmission of the hereditary characters (Weismann, 1885, p. 179), and Strasburger's studies of fertilization in Phanerogams appeared to afford proof that only the nucleus of the male cell is here concerned in the process of fertilization. As the contribution of the male and the female parents to the

hereditary equipment appears as a rule to be equal, and as the nuclei are the only equivalent structures in the male and the female gametes, the deduction seemed obvious that the hereditary tendencies must be carried by the nuclear substance alone. Nägeli, whose conception of a determinant idioplasm (1884) exercised considerable influence on Weismann's thought, was apparently the first to draw the conclusion that the hereditary substance must be present in equal amounts in the egg and the sperm, and must therefore be present in minimal quantity. His idioplasm, however, was a hypothetical substance extending as a network throughout all the cells of the body.[1] It was left to O. Hertwig, Strasburger, Kölliker, and Weismann to enunciate, all about the same time, the modern theory that the physical basis of heredity and development is to be sought in the nuclear substance, and more particularly in the chromosomes.

It is not necessary for our particular purpose here to follow up the further history of cytological discovery,[2] nor to enter into full details concerning Weismann's theory. We shall limit ourselves to considering such points as are of methodological interest, particularly in connexion with his theory of development.

Of fundamental importance is his conception of the germinal substance as the determiner of development. The chromatin granules, he tells us, are the most important constituents of the nucleus,

'for we must assume that it is their influence which determines the nature of the cell, which, so to speak, impresses it with the specific stamp, and makes the young cell a muscle-cell or a nerve-cell, which even gives the germ-cell the power of producing, by continued multiplication through division, a whole multicellular organism of a particular structure and definite differentiation, in short, a new individual of the particular species to which the parents belong. We

[1] Nägeli was also the first to take the dubious step of distinguishing the heredity-substance or idioplasm from the nutritive substance or trophoplasm—a distinction accepted and approved by Weismann, and by him explained on the principle of the division of labour (1902, i, p. 374).

[2] This is well treated in outline by E. B. Wilson, *The Cell in Development and Heredity*, 3rd ed., New York, 1925, chap. I.

call the substance of which these chromatin granules consist by the name first introduced into science by Nägeli, though only to designate a postulated substance which had not at that time been observed, but which he imagined to be contained within the cell-body—by the name *Idioplasm*, that is to say, a living substance determining the individual nature (εἶδος = form)'.[1]

The idioplasm accordingly exercises a direct formative influence upon the cell containing it, determining what sort of cell it will become. (This idea of active determiners working upon the more or less inert cell dates back to Darwin's theory of pangenesis (1868) and is prominent also in De Vries' theory of intra-cellular pangenesis (1889)). The idioplasm of the germ-cell—the hereditary or germinal substance proper—is conceived to be of a complex and orderly architecture, built up of self-propagating units or determinants, each of which is destined to be the formative agent of some particular part of the organism or of some particular group of cells. Weismann had been greatly impressed by the evidence that many single characters of the organism can vary quite independently of the rest and can be separately transmitted.[2] It seemed to him a necessary corollary that such independently heritable characters, or their constituent structural elements, must be represented in the germ-plasm by separate determinants. He concluded therefore that the germ-plasm must be compounded of determinant units, and that there must be a point-to-point correspondence between these units and the parts of the developing and adult organism which they produce. The theory of determinants is clearly stated in the following passage:

'I assume that the germ-plasm consists of a large number of different living particles, each of which stands in a definite relation to particular cells or kinds of cells in the organism to be developed, that is, they are "primary constituents" in the sense that their co-operation in the production of a particular part of the organism is indispensable, the part being *determined* both as to its existence and its nature by the

[1] English trans. of the *Vorträge* by J. Arthur Thomson and M. R. Thomson, under the title *The Evolution Theory*, London, 1904, vol. i, p. 287.

[2] The conception of 'unit characters', due originally to Nägeli, was elaborated particularly by H. de Vries in his *Intracellular Pangenesis*, Jena, 1889.

predestined particles of the germ-plasm. I therefore call these last *Determinants* (*Bestimmungsstücke*), and the parts of the complete organism which they determine *Determinates*, or hereditary parts' (ibid., p. 355).

The determinants are to be regarded not as specific chemical substances, however complex, but as living units, capable of assimilation, growth, and reproduction by division. Weismann here follows the physiologist Brücke[1] and others (H. Spencer and Darwin, for example) in supposing that all living matter is composed of invisibly minute units or biophors, each of which manifests the essential characteristics of life. Determinants may sometimes be single biophors, notably in unicellular organisms, but more often they are groups of biophors bound together in a higher unity. In their turn the determinants for the whole organism are bound up together to form an Id.

How do the determinants act? As they are essentially cell-determiners it is necessary that in the course of development they reach the cells or cell-groups on which they are to impose their particular character. For this to be possible it must be assumed that the Id has a definite and complex architecture, in which each determinant and each group of determinants has its proper and definite position. In the course of development the Id must be divided up in such a way that the determinants for the different regions of the body become separated and sorted out at the proper times and places. There must in other words be a progressive disintegration of the Id-complex by division, which proceeds in an orderly and predetermined fashion, until finally each separate kind of determinant is sorted out into the cells which it is predestined to transform. It is implied in this process that the Id can divide not only into identical parts (by 'Erbgleich' division), but also into unequal and dissimilar parts (by 'Erbungleich' division).

We may quote Weismann's own description of the process:

'If there is, then, a differential division of the ids and with them of the whole idioplasm, the germ-plasm of the fertilized ovum must

[1] 'Die Elementarorganismen', *S. B. Akad. Wiss. Wien*, xliv, 1861.

be broken up in the course of ontogeny into ever smaller groups of determinants. I conceive of this as happening in the following manner. In many animals the fertilized ovum divides at the first segmentation into two cells, one of which gives rise predominantly to the outer, the other to the inner germinal layer, as in molluscs, for instance. Let us now assume that this is the case altogether, so that one of the first two blastomeres gives rise to the whole of the ectoderm, the other to the whole of the endoderm: we should here have a differential division, for the developmental import (the "prospective" of Driesch) of the primitive ectoderm-cell is quite different from that of the primitive endoderm-cell, the former giving rise to the skin and the nervous system, with the sense organs, while the second gives rise to the alimentary canal, with the liver, &c. Through this step in segmentation, I conclude, the determinants of all the ectoderm-cells become separated from those of the endoderm-cells: the determinant architecture of the ids must be so constructed in each species that it can be segregated at the first egg-cleavage into ectodermal and endodermal groups of determinants. Such differential divisions will always occur in embryogenesis when it is necessary to divide a cell into two daughter-cells having dissimilar developmental import, and consequently they will continue to occur until the determinant architecture of the ids is completely analysed or segregated out into its different kinds of determinants, so that each cell ultimately contains only one kind of determinant, the one by which its own particular character is determined. This character of course consists not merely in its morphological structure and chemical content, but also in its collective physiological capacity, including its power of division and duration of life' (ibid., pp. 377–8).

When as a result of this orderly disintegration of the original complexity of the Id each kind of determinant reaches its allotted station in a particular group of cells, it becomes active and proceeds to shape the cells to their predestined form. To quote Weismann again:

'My conception of the manner in which the determinants become active is similar to that suggested by De Vries in regard to his "Pangens", very minute vital particles which play a determining part in his "pangen theory", similar to that filled by the determinants in my germ-plasm theory. It seems to me that the determinants must ultimately break up into the smallest vital elements of which they are composed, the biophors, and that these migrate through the nuclear

membrane into the cell-substance. But there a struggle for food and space must take place between the protoplasmic elements already present and the newcomers, and this gives rise to a more or less marked modification of the cell-structure. It might be supposed that the structure of these biophors corresponded in advance to certain constituent parts of the cell, that there were, for instance, muscle biophors, which make the muscle what it is, or that the plant-cells acquired their chlorophyllmaking organs through chlorophyll biophors. De Vries gave expression to this view in his "pangen theory", and I confess that at the time there seemed to me much to be said for it, but I am now doubtful whether its general applicability can be admitted. In the first place, it does not seem to me theoretically necessary to assume that the particles which migrate into the cell-bodies should themselves be chlorophyll or muscle particles; they may quite well be only the architects of these, that is to say, particles which by their co-operation with the elements already present in the cell-body give rise to chlorophyll or muscle substance' (ibid., pp. 379–80).

A little later on in the same discussion Weismann makes it clear that the determinants are not 'seed-grains' of individual characters, but co-determinants of the nature of the parts which they influence. In sum, he conceived the process of cell-differentiation to be as follows:

'At every cell-stage in the ontogeny determinants attain to maturity, and break up so that their biophors can migrate into the cell-bodies, so that the quality of each cell is thus kept continually under control, and may be more or less modified, or may remain the same. By the "maturity" of a determinant I mean its condition when by continual division it has increased in number to such a point that its disintegration into biophors and their migration into the cell-substance can take place' (ibid., p. 381).

The theory of the qualitative division of the nucleus as the basic phenomenon in differentiation, which Weismann worked out in such detail, had of course already been put forward by W. Roux,[1] on the strength of his own and Pflüger's experiments on the egg of the frog, and the early results of work on experimental embryology appeared for a time to corroborate it.

[1] *Ueber die Zeit der Bestimmung der Hauptrichtungen der Froschembryo*, Leipzig, 1883. See account by J. W. Jenkinson, *Experimental Embryology*, Oxford, 1909, pp. 17–19, and 158–62.

But, as is well known, the further progress of experimental research brought to light facts which were irreconcilable with the theory,[1] and it is now no longer tenable. Its place has been taken by the more definitely substantiated view that the 'germ-plasm' is represented by the complete set of chromosomes, and that the complete (double or single) set is present in all the cells of the organism, somatic and germinal alike. We shall consider this modern form of the germ-plasm theory—the theory of the gene—in the next Chapter. The theory of a germ-plasm present in all cells was also developed by de Vries and O. Hertwig, prior to the modern gene theory.[2] It is interesting to note in this connexion that in his paper of 1885 Weismann declared the theory of an omnipresent germ-plasm to be untenable. A propos of Nägeli's idioplasm, he pointed out how improbable it was that this substance could have the same constitution everywhere in the organism and during every stage of its ontogeny. For if this were so, how could the idioplasm effect the great differences which obtain in the formation of the various parts of the organism?[3] A very pertinent objection, which it is difficult to meet.

Although Weismann's theory of development can no longer be upheld in the present state of knowledge, the fundamental assumptions and conceptions underlying it are, many of them, still commonplaces of biological thought. We may summarize them as follows:

(1) For Weismann the ultimate goal was the explanation of vital phenomena in terms of physico-chemical action: he was a child of his time, and the materialist philosophy seemed to him the only possible foundation for scientific biology. Hence the emphasis laid on continuity of *substance*, and the formal solution offered of the problem of heredity on the basis of identity of starting-point. If the complex material configuration *a* brings about under standard conditions the

[1] See Wilson, 1925, pp. 1059–62.

[2] See Delage, 1895, sections on de Vries and Hertwig.

[3] *Essays upon Heredity*, 2nd ed., i, p. 184. He adopts, however, a less intransigeant attitude in 1902, see *Vorträge*, i, pp. 419 and 445 (Eng. Trans., i, pp. 382 and 407).

development of the specific organism A, and if this configuration is transmitted unchanged to serve as the starting-point of the next generation, it follows on the general principles of 'Mechanism' that there will be developed a replica of organism A, provided that the environment remains reasonably constant. So runs the materialistic argument. One main underlying assumption of Weismann's theory of heredity and development is then the correctness and adequacy of the mechanistic conception of life.

(2) Weismann realized, however, that the time was not ripe, nor knowledge sufficient, for the elaboration of a purely physico-chemical theory of heredity and development—he had some pertinent criticisms to make of the chemical epigenesis theory of Delage (1895).[1] He put forward his determinant theory as a first approach to a physiological analysis of the problems, believing himself justified in taking as given the properties of the elementary vital units which he conceived to be the components of all living substance. But he thought of the properties of his biophors and determinants as being the direct outcome of their material configuration.

(3) We must regard as fundamental to his theory the particulate conception of living things, according to which all living structures are built up of ultra-microscopic units or biophors, each of which manifests the essential characteristics of life—metabolism, growth, and movement. The origin of this general conception is obscure,[2] but it has a very long history; it has obvious relationship with the atomistic views both of matter and of living substance which can be traced back certainly as far as the Greeks; it is in a sense a biological atomism. The particulate conception is of significance even at the present day, for more than a trace of it remains in the

[1] *Vorträge*, i, pp. 439–40 (Eng. Trans., pp. 401–2).

[2] See historical account in E. Rádl, *Geschichte der biologischen Theorien*, ii, Leipzig, 1909, pp. 386–9. Wilson's account of the modern evolution of the idea is as follows: 'Brücke's suggestion, that the cell might be a congeries of bodies more elementary than itself, found a much fuller expression in Herbert Spencer's theory of physiological units, but it was Darwin's theory of pangenesis that laid the real basis for what followed in the works of de Vries, Wiesner, Weismann, and Hertwig,' *Wood's Holl Biological Lectures for 1898*, Boston, 1899, p. 3.

modern concept of the gene. It exemplifies very clearly a common methodological error, that of ascribing to an abstract part or component of an organism or a cell functions and capabilities which belong in reality only to the cell or organism as a whole (see below, pp. 153, 155).

There is a very interesting passage in the *Vorträge*, bearing on this point, which is worth while quoting in full:

'Some modern biologists deny that there is any hereditary substance *per se*, and believe that the whole of the germ-cell, cell-body, and nucleus together, effects transmission. But though it must be admitted that the nucleus without the cell-body cannot express inheritance any more than the cell-body without the nucleus, this is dependent on the fact that the nucleus cannot live without the cell-body; if it be removed from the cell and put, say, into water, it bursts and is dissolved. But the cell-body without the nucleus lives on, though of course only for a few hours or days, and its metabolism ceases only when it is brought to a standstill by the failure to replace by nutrition the used-up material. Thus the argument used by those who deny the existence of a hereditary substance would be paralleled if we denied that Man possesses a thinking substance, and maintained that he thinks with his whole body, and even that the brain cannot think by itself without the body.'[1]

Actually of course a 'heredity substance' is as much an abstraction as a 'thinking substance', and a man does think with his whole body, in the sense that the integrity of the body as a whole is an essential condition of the life and activity of the brain, the sense organs, and the neuromuscular system generally. As we shall see in more detail later (below, p. 155), elementary vital units such as biophors are likewise purely hypothetical and abstract constructions or figments of the intelligence; the only objects manifesting the full powers of life are living organisms, unicellular and multicellular. It is unjustifiable to fragment the living organism into lower units, to ignore the problem of 'composition' or wholeness, and to ascribe to these units the powers and capabilities which we know only as belonging to the organism as a whole. Weismann's determinants, by the

[1] i, p. 373; Eng. Trans., p. 340.

way, by means of which he purports to explain development and heredity, themselves manifest these phenomena (as do the chromosomes also)—a point which Aristotle made with regard to the 'seeds' of the pangenesists.[1]

(4) The peculiar weakness of the particulate conception of living things comes out very clearly when we consider the presumed activities of the determinants, which are themselves biophors or groups of biophors. They are conceived to be controllers or shapers of form, exerting upon the cytoplasm a modifying influence which cannot be clearly defined. With justice they might, though material, be likened to the entelechies of Driesch (see below, p. 102), for their mode of action is equally mysterious and equally far divorced from any known physiological process. The notion of *determinant* (in so far as it is taken to mean something more than a conditioning factor) is in fact a confused and unclear notion, deriving by way of the particulate conception from an underlying conviction of the reality of material determinism.

(5) Turning now to Weismann's theory of development regarded as a whole, we note at once that it is purely preformistic. To the developed organism there corresponds, point for point, the complex architecture of the Id. Development is brought about by the orderly disintegration of this complexity, so that, so far as the Id is concerned, development is a process of simplification which proceeds *pari passu* with the visible increase in complexity of the organism itself. The two processes are exactly complementary. What Weismann has done is to give an inverted redescription of the process of development in terms of a purely hypothetical complexity which simplifies itself. To translate the Id-theory into terms of the visible events it is only necessary to read 'potentiality'[2] of development for 'complexity' of the Id-architecture. The richer the potentiality, the less advanced the process of differentiation of visible structure, the more complex the structure of the idioplasm. The correspondence is strictly one of logical relation—hence the perfection

[1] See above, p. 17.

[2] Cf. Weismann's own expression 'Werde-Bedeutung' (*Vorträge*, i, p. 414).

of the theory. As is well known, Weismann had no difficulty in accounting for even the most astounding cases of regeneration by the simple and logical method of postulating a reserve idioplasm of the proper complexity. The theory is indefinitely extensible, and can surmount any difficulty; all that is necessary is to postulate for every new potentiality a new determinant or complex of determinants. But just in this logical perfection lies the essential weakness of the whole theory.

Why this type of reasoning makes so great an appeal to certain minds is an interesting psychological problem. It would seem that the mind jibs at the thought of a real evolution of complexity from simple beginnings, and seeks somehow to insert the complexity there at the beginning. But the plain evidence of the senses is that visible complexity does arise from visible simplicity, and there is nothing to be gained by a hypothetical inversion of the process.

It is perhaps hardly adequate to describe Weismann's theory of development as preformationist. The early preformationists regarded development as a simple unfolding of complexity already present; Weismann holds that development is essentially the progressive simplification of an original complexity; to the appearance of visible complexity there exactly corresponds a loss of complexity in the invisible formative germ-plasm.

(6) It is interesting to note how Weismann's theory enables him to deal with the problem of the harmony of development, of the proper co-ordination of developmental processes in time and space. For Weismann this is a pre-established harmony, fixed in its main lines by the orderly architecture of the idioplasm. The harmony or wholeness is there at the beginning and persists throughout development, being maintained by the structural orderliness of the germ-plasm. The normal equipment of germ-plasm suffices for normal development; if the conditions change and the organism must adapt itself, the emergency is met by groups of determinants held in readiness at the proper place for all likely eventualities. Again a redescription or translation in terms of hypothetical entities rather than a real explanation.

(7) It is hardly necessary to point out that Weismann's theory is essentially a morphologist's theory. He deals in terms of parts, of structures, and pays little attention to function or environment. The organism is regarded as a co-ordinated assemblage of unitary parts, each of which can vary independently of the others, each being represented in the germ-plasm by a special determinant or group of determinants, occupying its proper place in the germinal architecture. The relation between determinant and determinate is never stated in physiological terms, never linked up with known physiological processes. The theory is therefore non-physiological, and determinants are not merely abstractions, but morphological abstractions.

If we now sum up this elementary discussion and attempt to appraise the general value of Weismann's theory in its relation to the major problems, we may state our conclusions as follows: the theory is based explicitly upon a mechanistic conception of life; it offers a purely formal solution of the problems of differentiation, harmony, regulation, and heredity, in terms of the postulated activities of a hypothetical particulate substance, the idioplasm or germ-plasm, but this solution amounts to nothing more than a translation of the facts into what may appear to be, but is not, a simpler and more understandable form; it takes no account of the changing relationship between form and function during development, and it is pre-eminently a morphological, non-physiological theory, working in terms of abstract structural units of different grade, and their relations one to another.

Weismann does, however, take into consideration the relation between phylogeny and ontogeny which finds expression in the fact of recapitulation. His theory allows for the origin of new determinants in the course of evolution, and the consequent appearance of new characters in ontogeny. Speaking of his determinants and groups of determinants, he writes:

'That they do not enter into activity all at once, but successively take their part in development, seems to me a necessary consequence

of their successive origin in the phylogeny; and the ontogeny, as we shall see later, arises through a modified condensation of the phylogeny. Now since every new determinant that arises in the course of phylogeny can only develop by division and subsequent variation from the determinants which were previously active at the same place in the organism, it is quite intelligible that later on, when the phylogeny has been condensed in the ontogeny, they should not enter upon their active stage at the same time as their phyletic predecessors, but after them.'[1]

In the foregoing discussion we have dealt only with the broad outlines of Weismann's theory, and mainly with the theory as set out in the first edition of the *Vorträge* (1902). Much detail has accordingly been omitted, and it should be noted that Weismann modified some of his views in the light of advancing knowledge.[2] The main underlying ideas remain however the same, and it is his earlier writings that are historically important.

[1] Eng. Trans., i, p. 405.
[2] See the third edition of the *Vorträge*, 1913.

V

THE THEORY OF THE GENE

WEISMANN held that each chromosome must contain at least one full set of determinants (and in most cases several sets). He arrived at this conclusion in a perfectly logical way. He argued that if the chromosomes were different, so that each held only the determinants for a particular part of the body or for a particular set of characters, it would be difficult or impossible for the fertilized egg to receive invariably, as clearly it does receive, a complete set of determinants. It would be necessary to assume, for instance, that at least the haploid set of chromosomes contained the determinants for the whole organism, for if it did not, but bore only those for certain parts, it would be a rare occurrence that the egg and sperm uniting to form the zygote carried exactly complementary groups of determinants and a perfect embryo resulted. But each haploid group contains chromosomes of maternal and of paternal origin, which we have no justification for supposing to be always complementary to one another; hence it seems to follow that, in order to account for the fact that a complete organism invariably arises from the fertilized egg, each chromosome must contain all the determinants necessary for complete development, and the fertilized egg many such sets of determinants.[1]

But Weismann overlooked one possibility—that prior to reduction the homologous maternal and paternal chromosomes should pair and that at reduction they should separate, so that each gamete would receive a complete haploid set of chromosomes, as a rule of mixed paternal and maternal origin, and each zygote two complete sets.

Near the beginning of the present century cytological research showed that this possibility was actually realized in certain cases, and the view that reduction was preceded by conjugation of homologous chromosomes of maternal and

[1] *Vorträge*, i, pp. 378–81 (Eng. Trans., pp. 345–8).

paternal origin was rapidly generalized and widely accepted. About the same time, Boveri's classical experiments with dispermic sea-urchin eggs furnished clear evidence that the chromosomes were in fact qualitatively different—as indeed Roux (1883)[1] had deduced on theoretical grounds—and that for normal development one complete haploid set was the minimum necessary. The other factor which, combined with the new cytological discoveries, led to the theory of the gene, was of course the re-discovery in 1900 of the Mendelian principles of heredity.

Sutton (1902 and 1903) appears to have been the first to draw the complete parallel between the cytological facts and the Mendelian results, and to explain Mendelian segregation as due to the separation of maternal and paternal chromosomes at reduction and their random distribution to the gametes. It is useful here to quote Wilson's account of Sutton's views:

'In brief summary Sutton's conclusions were as follows:

'(1) The somatic or diploid chromosome-groups are made up of two equivalent chromosome-groups or series, one of maternal derivation and one of paternal (Van Beneden, Boveri, Montgomery).

'(2) The chromosomes retain their morphological individuality and are genetically continuous throughout the life-cycle (Van Beneden, Rabl, Boveri).

'(3) The process of synapsis consists in the union or conjugation of corresponding or homologous maternal and paternal chromosomes which in the reduction division disjoin, pass to opposite poles of the spindle, and thus always into different germ-cells (Montgomery, Sutton).

'(4) Each chromosome plays a definite part in the determination of development (Boveri).'

'To the foregoing Sutton added the following theoretic postulates:

'(5) A given size-relation is characteristic of the physical basis of a definite set of genetic units. Each chromosome of any haploid series in the species has a homologue in any other series, and these homologous members of each pair "cover the same field" in development.

[1] *Ueber die Bedeutung der Kerntheilungsfiguren*, Leipzig, 1883. Reprinted in *Gesammelte Abhandl.* (No. 17), Leipzig, 1895.

This means, in more modern terminology, that the synaptic mates contain the physical units (factors or genes) that correspond to the Mendelian allelomorphs.

'(6) "In the reduction-division the position of the chromosome-pairs or bivalent chromosomes in the equatorial plate is purely a matter of chance—that is, any chromosome-pair may lie with maternal or paternal chromatid toward either pole irrespective of the positions of other pairs—and hence a large number of different combinations of maternal and paternal chromosomes are possible in the mature gametes of an individual."

'Sutton clearly showed that the formulas of Mendelian heredity generally (as then known) could be applied without alteration alike to the hypothetical "factors" or "genes" and to the chromosomes; and that the combinations, segregations, and recombinations of the former are paralleled by those of the latter. Sutton also foreshadowed the modern theory of linkage, pointing out the necessity for the assumption that "some chromosomes at least are related to a number of different allelomorphs"; that "all the allelomorphs represented by any one chromosome must be inherited together"; and further, that "the same chromosome may contain allelomorphs that may be dominant or recessive independently" ('03, p. 240). This, as far as it goes, is in all essentials identical with the results afterwards worked out by Morgan and his co-workers in genetics which demonstrate that in the case of *Drosophila* at least *the number of linkage groups is the same as the haploid number of chromosomes*."[1]

The extensive and elaborate breeding experiments carried out from about 1910 onwards by Morgan and his school disclosed many interesting facts about the inheritance of a large number of mutations occuring in the fruit-fly *Drosophila*, and enabled the results to be expressed in numerical ratios. For the interpretation of these results Morgan utilized and extended the conception of Sutton that Mendelian inheritance is bound up with the distribution of the chromosomes in reduction.

It is not necessary for our special purpose here to enter into details regarding Morgan's theory of the gene, nor to concern ourselves with the ingenious hypotheses of crossing-over, interference, lethal factors, and so on, by means of which

[1] Wilson, 1925, pp. 926–7.

deviations from the expected numerical ratios are explained.[1] What we are concerned with are the fundamental postulates of the theory and the justification for them.

Morgan sums up the essentials of the theory as follows:[2]

'The theory states that the characters of the individual are referable to paired elements (genes) in the germinal material that are held together in a definite number of linkage groups; it states that the members of each pair of genes separate when the germ-cells mature, in accordance with Mendel's first law; it states that the members belonging to different linkage groups assort independently in accordance with Mendel's second law; it states that an orderly interchange—crossing-over—also takes place, at times, between the elements in corresponding linkage groups; and it states that the frequency of crossing-over furnishes evidence of the linear order of the elements in each linkage group and of the relative position of the elements with respect to each other.'

Another protagonist of the gene theory is even more sweeping in his statements.

'The hereditary constitution of at least all higher organisms', writes Professor J. S. Huxley,[3] 'consists of a number of units (factors or genes), each of which may exist in a number of forms (allelomorphs); these genes exist in definite proportions, and are arranged in a definite order; the whole gene-complex is divided up among the separate chromosomes, which in *Drosophila* have been shown to correspond to the linkage-groups established by genetic experiments.'

It would seem at first sight that we have here to do with a mere variant of the Weismannian idea of determinants, that the genes or factors are the sole determiners of the characters whose names they bear, and there is in fact a close analogy between the two concepts. The existence of genes is however deduced on quite different grounds, and Morgan

[1] These are critically dealt with by H. Stieve, 'Neuzeitliche Ansichten über die Bedeutung der Chromosomen, unter besonderer Berücksichtigung der Drosophilaversuche', *Ergebn. Anat. Entwick.* xxiv, 1923, pp. 491–587. See also J. Dembowski, 'Zur Kritik der Faktoren- und Chromosomenlehre', *Zts. indukt. Abstamm. Vererbungslehre*, xli, 1926, pp. 216–47.

[2] T. H. Morgan, *The Theory of the Gene*, New Haven, 1926, p. 25.

[3] *Nature*, Dec. 25th, 1926, p. 903. See also H. S. Jennings, *Prometheus*, London, n.d., for a bold and picturesque account of the theory.

specifically denies that they can be regarded as equivalent to representative particles.

When a female *Drosophila* with red eyes is mated with a male having white eyes (a mutation), the F 1 generation all have red eyes, and the F 2 generation show a ratio of three reds to one white—an ordinary case of Mendelian inheritance. It can be interpreted on the assumption that in the F 1 hybrid 'something for red eyes has separated from something for white eyes'. We are told also that 'We may express these factorial relations in another way by saying that a germ cell that produces white eyes differs from a germ cell that produces red eyes by one factor-difference. We think of this difference as having arisen through a factor in the red-eyed wild fly mutating to a factor for white.'[1]

Now the interpretation offered in this last sentence does not seem to be a necessary deduction from the facts, and it reveals to us the fundamental assumption or postulate of the whole theory. Let us accept the evidence that the mechanism of Mendelian inheritance is bound up with the chromosomes; let us further agree that the chromosome *A*, which is associated with the production of red eye, differs from the chromosome *A'*, which is in some way responsible for the appearance of white eye. The facts appear to justify, or at least to be consistent with, these conclusions. What is the nature of the difference between these two chromosomes? Morgan assumes that the difference is particulate, that one locus of chromosome *A'* differs from the corresponding locus of chromosome *A*, and that these loci can in practice be treated as detachable and movable material units. We get at once from this primary assumption the whole elaborate theory of the gene. But the difference between the two chromosomes may quite well be a slight though discontinuous chemical or stereochemical change affecting the chromosome as a whole.[2] We do not ascribe the difference in properties

[1] Morgan, Sturtevant, Muller, and Bridges, *The Mechanism of Mendelian Heredity*, revised edition, New York, 1922, p. 262.

[2] Equally well it may affect *principally* one particular section or locus of the chromosome (see below, p. 281). The point is that it should not be hypostatized as a definite and independent *particulate unit*, which is necessarily a pure abstraction.

between two chemical isomers to a *particulate* difference in their constitution, but to a different arrangement of their constituent atoms. Nor do we attempt to pin down the difference in properties to one constituent of the molecule.[1] Why should we then adopt the particulate explanation in the case of differing chromosomes?

The original ground for assuming that the difference is a particulate one appears to be that the effect shown by the developed fly is a definite and discontinuous change manifested primarily in one character. It is natural to think that a discontinuous effect of this kind has a particulate cause in the germ-cell. The gene theory in its original form was linked up with the concept of unit characters. The process of thought is the same as that which led Weismann to postulate the existence of separate determinants to account for the independent heritability of small definite, discontinuous characters. But the conception does not emerge inevitably from the facts—another mode of explanation is equally possible. The gene theory is therefore only a hypothesis, and the existence of genes as concrete things cannot be certainly demonstrated from arguments of this character.

It is interesting to note that the development of genetic research has shown that the relation of gene to character is not the simple one of determinant to determinate, and the concept of unit characters is accordingly losing its importance.

'Mendelian heredity has taught us that the germ cells must contain many factors that affect the same character. Red eye color in Drosophila, for example, must be due to a large number of factors, for as many as 25 mutations for eye color at different loci have already come to light. Each produced a specific effect on eye color; it is more than probable that in the wild fly all or many of the normal allelomorphs at these loci have something to do with red eye color. One can therefore easily imagine that when one of these 25 factors changes, a different end result is produced, such as pink eyes, or vermilion eyes, or white eyes or eosin eyes. Each such color may be the product of 25 factors (probably of many more) and each set of 25 or more differs

[1] See Delage (below, p. 82).

from the normal in a different factor. It is this one different factor that we regard as the "unit factor" for this particular effect, but obviously it is only one of the 25 unit factors that are producing the effect. However since it is only this one factor and not all 25 which causes the difference between this particular eye color and the normal, we get simple Mendelian segregation in respect to this difference.' [1]

Conversely, any one factor may affect more than one character; that for rudimentary wings may affect also the legs, the number of eggs laid, and the general viability of the organism.

'The genetic evidence', writes Morgan in his latest book,[2] 'has abundantly shown that when a single gene is changed, the end-product may be affected in many ways. We select the most important, and for our purposes, most convenient change and identify it as the immediate product of the new gene. But as is well understood, this is only a useful method in studying the inheritance of the genes. It is perfectly well known that, besides certain major effects, there are many accompanying effects also present involving all parts of the body, and this result is entirely consistent with the theory that all the parts are the products of all the genes.'

It is clear then that there is no simple relation between character and factor, and the argument from the genetic behaviour of the character to the existence of the factor or gene loses much of its force.

Throughout the whole of the *Drosophila* experiments, we have to do with the hereditary behaviour of small distinct *differences* (mutations) from the normal. There is much solid evidence that these differences are associated with differences between pairs of chromosomes.

To quote Morgan again:

'The germ cells may be thought of as a mixture of many chemical substances, some of them more closely related to the production of a special character, color for example, than are others. If any one of the substances undergoes a change, however slight, the end-product of the activity of the germ cell may be different. All sorts of characters might be affected by the change, but certain parts might be more

[1] Morgan and others, op. cit., pp. 262–3.
[2] *Experimental Embryology*, New York, 1927, p. 207.

conspicuously changed than are others. It is these more obvious effects that we seize upon and call unit characters.'[1]

That is a reasonable and objective statement, but the gene theory goes very much farther. In effect it 'reifies' or endows with material existence what are merely differences, and it does this by postulating a gene for every heritable difference found. It may be said that this is an unfair statement, and that the gene for each atypical character, each mutation, is merely a modification or mutation of the gene for the typical character,[2] and does not represent the modification *per se*. But this merely means that a normal gene has already been postulated to account for the typical character—and both genes are equally hypothetical.

The postulation of separate genes for each distinguishable difference and of the equivalent normal genes leads to very great complications. Take the case, described in the quotation on p. 59 above, of the twenty-five factors required for the production of normal eye-colour in *Drosophila*. Let us grant that there are in fact twenty-five different modifications of the various chromosomes concerned, each of which can bring about a definite, observable, and constant abnormality in eye-colour. The facts may legitimately bear that interpretation (though it is difficult to concede that twenty-five distinct shades of colour can be accurately distinguished in the eye of *Drosophila*). Is it really necessary to assume that each of these differences is localized in a particular section of the chromosome in the shape of a mutant gene, *and that it has a counterpart in the 'normal' chromosome in the shape of a normal gene*? This is surely a breach of the good old medieval rule that 'Entia non sunt multiplicanda praeter necessitatem'. The result obtained—that at least twenty-five factors or genes (whose nature is completely unknown, and whose relation to ascertained physiological processes is completely

[1] Morgan and others, op. cit., p. 264.

[2] Cf. F. A. E. Crew: 'A gene is a particular state of organization of the chromatin at a particular point along the length of a particular chromosome. It is a particular area or locus of the chromosome in a particular state. One particular condition of this chromatin can be replaced by others and with each change another gene appears', *Nature*, Nov. 19th, 1927, p. 733.

mysterious) are concerned in the production of normal eye-colour—is frankly incredible. Eye-colour in *Drosophila* is, physiologically speaking, a resultant of the mixture of two pigments only—wine-red and ochre-yellow. 'The eyes of the eye-color mutants, "eosin-miniature", "eosin-vermilion", "pink", "purple", "ruby", "sepia", "tinged", "vermilion", and "white", have the same structures and pigments possessed by the normal eye, differing only in the amount and distribution of the pigment. The pigments are much reduced in "tinged", "eosin-vermilion", and in the female of "eosin-miniature".'[1] It seems highly doubtful that such an elaborate mechanism of mutant genes is necessary to induce such relatively simple changes, and it borders on the miraculous that the production of the normal amount and distribution of the two pigments concerned should require the combined action of twenty-five 'and probably many more' normal genes. Generalizing from this example, it would seem that there must exist as many normal genes as there are separately distinguishable characters, and as many mutant genes as there are mutations of these characters, that is to say, an unlimited number of genes. The hypothesis crumbles under its own weight.

We are not, however, primarily concerned here with a detailed criticism of the gene theory, especially as it has clearly not yet reached the term of its evolution. Our object has merely been to show that the genes are purely hypothetical units—convenient (or inconvenient ?) fictions invented to account for the very complex hereditary behaviour of mutant characters in *Drosophila*. As such they have a certain interpretative and heuristic value, provided that their purely conceptual and hypothetical character is clearly borne in mind. That the *Drosophila* results are interpretable on a pure and abstract factorial hypothesis, quite apart from any identification of the factors with material and unitary parts of the chromosomes, is of course freely admitted by Morgan, who writes, 'The factorial theory as such deals with the behavior

[1] O. A. Johannsen, 'Eye Structure in Normal and Eye-mutant Drosophila', *Journ. Morph. Physiol.*, xxxix, 1924, pp. 337–50.

of its factors in an abstract way, quite apart from any material basis of which they may happen to be composed. In this way, it may measure their constancy, segregation, linkage, &c.'[1]

To arrive at a just estimate of the value of the gene theory in relation to the major problems of development and heredity, we cannot do better than follow the lead of the late Professor W. Johannsen, himself the inventor of the term 'gene', and a most distinguished worker in genetics. In a short but fundamental paper[2] he lays his finger on the limitations of modern genetical theory, and assesses its general significance in masterly fashion. We shall here reproduce his views in some detail.

After pointing out that the theories of heredity propounded by Darwin, Galton, Weismann, De Vries, and the early Mendelians were profoundly morphological, dealing as they did with *parts* of the organism regarded as units in inheritance, he shows that the later concept of unit *characters* is also a morphological notion, implying a reification of qualities, and can now no longer be upheld. What is required is a physiological or 'chemico-biological' formulation of the facts.

'It was undoubtedly a step forward to leave the notion of unit-*parts* in favour of the notion of unit-*characters*. Now this notion too is absolutely untenable. Nowadays each of Bateson's allelomorphs are not regarded as a kind of germ ("Anlage") for a corresponding unit-character. My term "gene" was introduced and generally accepted as a short and unprejudiced word for unit-factors in the—as to heredity—essential constitution of gametes and zygotes, but originally I was somewhat possessed with the antiquated morphological spirit in Galton's, Weismann's and Mendel's viewpoints. From a physiological or chemico-biological standpoint we must a priori in characters or developed parts of organisms see *Reactions* of the (I should say genotypical) constitution belonging to the zygote in question; and from this point of view *there are no unit-characters at all*! Undoubtedly all scientific geneticists now are or ought to be in accord as to this matter' (p. 136).

In genetics we have to do

'with such genotypical units as are separable, be it independently

[1] Morgan and others, op. cit., p. 278.

[2] 'Some Remarks about Units in Heredity', *Hereditas*, iv, Lund, 1923, pp. 133–41.

or in a more or less mutual linkage. Certainly by far the most comprehensive and most decisive part of the whole genotype does not seem to be able to segregate in units; and as yet we are mostly operating with "characters" which are rather superficial in comparison with the fundamental Specific or Generic nature of the organism. . . . We are very far from the ideal of enthusiastic Mendelians, viz. the possibility of dissolving genotypes into relatively small units, be they called genes, allelomorphs, factors or something else. Personally I believe in a great central "something" as yet not divisible into separate factors. The pomace-flies in Morgan's splendid experiments continue to be pomace-flies even if they lose all "good" genes necessary for a normal fly-life, or if they be possessed with all the "bad" genes, detrimental to the welfare of this little friend of the geneticists.

'Disregarding this (perhaps only provisional?) central "something" we should consider the numerous genes, which have been segregated, combined or linked in our modern genetic work. What have we really seen? The answer is easily given: We have only seen *Differences*. The famous relation 3 : 1 (1 : 2 : 1) indicates one single point of difference, the ratio 9 : 3 : 3 : 1 two points, and so on. Dominance does not at all indicate the presence of some positive unit, just as little as Recessivity indicates the lack of any unit. This is clearly seen, for instance, in Nilsson-Ehle's oats-crossings, where one Mendelian unit may be responsible for one dominant and one or two recessive characters, also in such cases where dominance or recessivity is dependent upon external conditions, as in some *Drosophila*-experiments' (p. 137).

Further, 'When we regard Mendelian "pairs", Aa, Bb and so on, it is in most cases a *normal* reaction (character) that is the "allel" to an *abnormal*' (p. 138).

As to the nature of the difference between the pairs:

'There is at present scarcely any doubt about the theory, that "Mendelian" factors are in some way bound in or to the chromosomes. The morphological view regards them as formed particles (say "morphs" ad modum "allellomorphs") of the chromosomes, an old Weismannian idea—mutatis mutandis. From a physiological standpoint we may prefer to regard local conditions (say "chemisms") in or on the chromosomes as responsible for those units' (p. 138).

Finally, Johannsen raises a serious doubt as to the evolutionary significance of the Mendelian phenomena:

'To my mind the main question in regard to these units is this: Are the experimentally demonstrated units anything more than ex-

pressions for local deviations from the original ("normal") constitutional state in the chromosome? Is the whole of Mendelism perhaps nothing but an establishment of very many chromosomical irregularities, disturbances or diseases of enormously practical and theoretical importance but without deeper value for an understanding of the "normal" constitution of natural biotypes? The Problem of Species, Evolution, does not seem to be approached seriously through Mendelism nor through the related modern experiences in mutations' (p. 140).

There are two points deserving of special notice in this considered judgement of Johannsen's: (1) that Mendelian heredity has to do with the inheritance of *differences* from the normal, mostly superficial differences and often degenerative or pathological, and (2) that in addition to these differential characters, which mendelize, there is the whole body of the main characters of the organism, forming a central group which is apparently transmitted *en bloc*. Let us consider these points in further detail.

(1) That the Mendelian characters are mainly superficial, affecting the coloration of the organism, or relating mainly to slight bodily peculiarities, is to some extent admitted by Morgan and his school, but they in no way agree that the scope of the Mendelian principle is limited to superficial characters.

'It is true', writes Morgan, 'that by far the greatest number of characteristics that students of Mendelian inheritance have concerned themselves with relate to superficial differences, such as shades of color or slight differences in the length or breadth of characters that are relatively unimportant for the individual. The explanation of this procedure is obvious enough, for it is just these slight differences that do not interfere with the survival of those individuals that are necessary to the geneticists. But there is no line that can be drawn between these trivial differences and those that are more significant and fundamental. Even such a fundamental property as symmetry has been shown to depend on a single Mendelian gene, as when the bilateral flower of the snapdragon changes to a peloric flower with radial symmetry. So far as Mendelian factors are concerned, the evidence is quite sufficient to show the erroneousness of the view that Mendelian genes are concerned only with trifling differences' (p. 727).[1]

[1] 'Mendelian Heredity in relation to Cytology', in Cowdry, *General Cytology*, Chicago, 1924.

The point is discussed at some length in his book *The Physical Basis of Heredity* (Philadelphia and London, 1919), and it is worth while to quote the relevant passage in full:

'It has been sometimes stated', he writes, 'usually by the opponents of Mendel's theory, or by advocates of doctrines of evolution that appeared to be compromised by the Mendelian conception of "unit factors", that Mendelism deals only with such superficial characters as the color of flowers or the hair color of mammals. This statement contains an element of truth in so far as it covers most of the kinds of characters that students of heredity find most convenient to study; but it contains an entirely false inference as to the limitations of Mendelism. The issue involved is this: changes in superficial characters are not so likely to affect the ability of the organism to survive as are changes in essential organs; hence they are the best kind of hereditary characters for study. But there is no evidence that such superficial characters are inherited in a different way from "fundamental" characters, and there is evidence to the contrary. A common class of characters showing perfect Mendelian behavior are so-called lethals that destroy the individual when in homozygous condition. There can be no question as to the fundamental importance of such factors. Between these extreme cases and the superficial shades of eye color, for example, all possible gradations of structure, physiological and pathological, are known. The only possible question that might be seriously raised is whether these characters are all losses or deficiencies, while progressive advances may belong to a different category. This may be a serious question for the evolutionist, but has nothing to do with the problem that concerns us here' (p. 36).

It is admitted then, that with the exception of the lethal factors, the characters showing Mendelian behaviour are minor characters. The reason for this is, however, alleged to be that these are the most convenient characters to study, since mutations of greater scope are not as a rule viable.

But there is a much more obvious reason for the limitation of the Mendelian principle. Mendelian heredity is shown only in sexual reproduction, and it can be demonstrated only if there are one or more differences between the conjugating gametes: obviously it cannot occur at all if fertile union between the divergent gametes is impossible. The experi-

mental demonstration of the principle is therefore limited to cases where the difference between the parental types is not too great to prevent successful fertilization and normal development. It relates only to hereditary *differences*, and these differences can by the nature of the case be only differences so unimportant that they do not interfere with normal crossing. I say 'unimportant' rather than 'slight', for quite striking differences can be inherited in Mendelian fashion, e.g. dwarfness or tallness in peas; such differences are, however, never so considerable as to be developmentally incompatible with the realization of the specific form. The argument from lethal factors advanced by Morgan is not in the least convincing. The lethal factor is a figment invented to account for the non-appearance of certain factorial groupings, and the occurrence of such abortive broods or parts of broods (in cases where they are demonstrated to occur) merely illustrates the fact that certain combinations are infertile or non-viable, presumably because they include factors mutually incompatible. Dembowski's comments on the subject of lethal genes are very much to the point:

'The lethal factors especially', he writes, 'help us to recognize the true nature of the gene. Death is an extremely complicated phenomenon, which may depend upon an innumerable host of circumstances of the most diverse kind. When the cause of death is simply called a "lethal gene", this shows us clearly what a gene really is. We have already come to the conclusion that a gene cannot be material. Now we have the solution that fulfils that condition. *The gene is a word*, which enables a complicated happening to be briefly denominated.' (op. cit., p. 244).

We may safely say then that the Mendelian principle, so far as the definite experimental evidence goes, is necessarily limited to the narrow field of fertile inter-crossing. Such differences as are not incompatible with fertile crosses may with justice be called 'unimportant' or 'superficial' in relation to the normal specific form and characteristics.

It is interesting to note that Morgan is inclined to admit that many of the differences whose hereditary behaviour has been studied on Mendelian lines, especially in *Drosophila*, are

deficiency variations,[1] and after studying the pictures of the semi-aborted and abnormal flies which make up the bulk of his mutations, one can only agree with him. In general, as he himself says, the mutant types of *Drosophila* are weaker and less well adapted than the normal wild type.[2]

The extension of the Mendelian principle to characters other than those which can be studied in actual crosses is of course based on the general conception that the chromosomes constitute the physical basis of heredity. The argument runs somewhat as follows. The Mendelian factors are certainly borne by the chromosomes, and their behaviour can be interpreted by what we know of the distribution of the chromosomes in maturation, reduction, and fertilization. The chromosomes appear to be the only possible vehicles for the transmission of the characters of the organism as a whole, since they are the only equivalent structures in the male and female gametes, and the contribution of both parents to the hereditary equipment of the offspring appears to be equal. Hence it would seem that what is true of one set of characters should be true of the others, since all are borne by the chromosomes. We arrive therefore at the conception of a genetic constitution, consisting of a large number of factors, like those demonstrated by Mendelian research, and responsible between them—with the co-operation of the cytoplasm and of environmental conditions—for the inheritance and development of all the characters of the organism.

There is, however, contained in this argument a curious *petitio principii*, which has as a rule escaped notice, though recently it has been pointed out by Winkler.[3] The logical slip is the assumption that the paternal and maternal contributions are of equal importance. For how can this be proved? In all breeding experiments we can deal only with differences, and only with such differences as are not incompatible with fertile inter-crossing. The great bulk of characters is necessarily common to both parents, and about

[1] See quotation on p. 66. [2] Morgan, 1926, p. 65.

[3] H. Winkler, 'Ueber die Rolle von Kern und Protoplasma bei der Vererbung', *Zts. Indukt. Abstamm. Vererbungslehre*, xxxiii, 1924, pp. 238–52.

each parent's contribution to the inheritance of what is common to both, breeding experiments can obviously tell us nothing. Experimental work can deal only with the inheritance of minor characters or of minor variations of major characters. Accordingly, so far as the facts go and strict logic carries us, inheritance of the main characters might be purely maternal, and involve not only the nuclear apparatus but very intimately the cytoplasm, which is practically absent in the majority of male gametes. The facts under consideration do not of course prove this unilateral inheritance, but they can certainly not be used to demonstrate that the main characters are derived in approximately equal measure from both parents.[1] This being so, the logical argument for the extension of the gene theory to *all* characters of the organism falls to the ground, and the question remains completely open.

(2) Here then is the point of Johannsen's suggestion, that in addition to all the separable, mendelizing characters, which can be treated in terms of separate factors, there must be postulated a 'great central "something", as yet not divisible into separate factors'. That it will ever be so divisible seems highly improbable.

We must conclude then, until further evidence is forthcoming—if it ever is—that the scope both of the Mendelian principle and of the gene theory is limited to such rather superficial variations as can be dealt with by experimental breeding. The direct contribution which genetic experiment and genetic theory make to the main problem of heredity—the reproduction of specific type, apart from minor deviations—is therefore a strictly limited one; the fundamental problem is in fact hardly touched.

To the problems of development, of individual ontogeny, the gene theory admittedly makes no contribution at all; rather does it add complications. Let us hear Morgan on the subject:

'Between the characters, that furnish the data for the theory, and the postulated genes, to which the characters are referred, lies the

[1] This important point is more fully developed in Chapter XIV below.

whole field of embryonic development. The theory of the gene, as here formulated, states nothing with respect to the way in which the genes are connected with the end-product or character.' [1]

Or again,

'The cause of the differentiation of the cells of the embryo is not explained on the factorial hypothesis of heredity. On the factorial hypothesis the factors are conceived as chemical materials in the egg, which, like all chemical bodies, have definite composition. The characters of the organism are far removed, in all likelihood, from these materials. Between the two lies the whole world of embryonic development in which many and varied reactions take place before the end-result, the character, emerges. Obviously, however, if every cell in the body of one individual has one complex, and every cell in the body of another individual has another complex that differs from the former by one difference, we can treat the two systems as two complexes quite irrespective of what development does, so long as development is orderly.' [2]

The gene theory deals with the explanation of *differences* between two or more ontogenies, not with development itself. The gene theory is therefore in no way a theory of development. The introduction of the gene concept into the general theory of development is likely to lead merely to confusion, since, as we have seen reason to conclude, the gene is a purely hypothetical unit, having like Weismann's determinants no corporeal existence, and invented for a very different purpose than the explanation of the developmental process.

It is in fact peculiarly difficult to harmonize the modern theory of the germ-plasm with the facts of embryonic differentiation, for according to that theory the germ-plasm is the whole chromosomal complex, and this complex occurs apparently unchanged in every cell of the body. Weismann's theory of a qualitative division of the nucleus and an orderly disintegration of the formative germ-plasm was much more appropriate, but unfortunately it was definitely negatived by the facts. There seems no escape from the conclusion that the chromosomal apparatus is divided only quantitatively, and is handed on unaltered at every mitosis. The chromo-

[1] Morgan, 1926, p. 26. [2] Morgan and others, 1922, p. 280.

somes appear therefore *prima facie* to have nothing whatever to do with cellular differentiation, which in fact affects solely the cytoplasm.

Attention has been called to this difficulty particularly by Dobell, with special reference to the cycle of changes exhibited by the life-history of the sporozoon *Aggregata eberthi*.[1] He writes:

'In *Aggregata* we see great individual diversity associated with apparently complete identity of chromosomic constitution. From generation to generation the forms and functions of the animal change in an orderly sequence, while the chromosomes remain unchanged. They are the constants in a varied series of developmental stages. It is therefore obvious that if any internal "factor" in such a sequence of forms "determines" the manifestation of any particular bodily character at any stage, this factor must be somehow associated not with the chromosomes but with some extra-chromosomic constituent of the organism. The organism models itself and acts not because of its chromosomic components but in spite of them.

'As there is thus no reason whatsoever to suppose that any chromosome—or part of a chromosome—in *Aggregata* is correlated with or determines the manifestation of any character in the individual actually possessing it, it follows that there is no justification for the further supposition that the chromosomes are specially concerned in the hereditary transmission of any character from any individual to its progeny' (p. 184).

The same arguments apply also to differentiation in the tissue cells of Metazoa.

The relation of the modern germ-plasm theory to the physiology of development is also discussed—and in a very able way—by F. R. Lillie,[2] who writes:

'It is apparently not only sound, but apparently almost universally accepted genetic doctrine to-day that each cell receives the entire complex of genes. It would, therefore, appear to be self-contradictory to attempt to explain embryonic segregation by behavior of the genes which are *ex hyp.* the same in every cell' (p. 365).

There is a complete divergence between the methods and

[1] Clifford Dobell, 'The Chromosome Cycle of the Sporozoa considered in Relation to the Chromosome Theory of Heredity', *La Cellule*, xxxv, 1925, pp. 167–92.

[2] 'The Gene and the Ontogenetic Process', *Science*, lxvi, 1927, pp. 361–8.

postulates of genetics and the physiology of development, which is not likely to result in the victory of the geneticists.

'The present postulate of genetics is that the genes are always the same in a given individual, in whatever place, at whatever time, within the life-history of the individual, except for the occurrence of mutations or abnormal disjunctions, to which the same principles then apply. The essential problem of development is precisely that differentiation in relation to space and time within the life-history of the individual which genetics appears implicitly to ignore. The progress of genetics and of physiology of development can only result in a sharper definition of the two fields, and any expectation of their reunion (in a Weismannian sense) is in my opinion doomed to disappointment. Those who desire to make genetics the basis of physiology of development will have to explain how an unchanging complex can direct the course of an ordered developmental stream' (p. 367).

A special study has been made by Hance[1] to determine whether any definite relation can be observed between differentiation of cell and differentiation of chromosomal complex—with definitely negative results.

'The morphological data', he writes, 'on the behavior of the chromosomes in the developing embryo, although admittedly scant, has [*sic*] so far given no clue to the manner in which the chromosomes may contribute their potentialities to the growing organism. Before a study of somatic chromosomes had been made it seemed reasonable to expect to find the various highly differentiated cells of the body with chromosome numbers, morphology or behavior at variance both with those found in other tissues and with the specific number and general characteristics found in the gonads. This has been found not to be the case in at least three forms, the pig, the evening primrose and the chick. . . . In general the chromosome situation in the soma seems to be entirely similar to that found in the unreduced gonad cells' (p. 445).

This is very difficult to explain on the theory that the chromosomes are the structures mainly responsible for heredity and development, and Hance's tentative hypothesis quoted below sounds very much like an attempt to bolster it up at all costs.

'In view of the entire similarity', he writes, 'of the somatic and

[1] R. T. Hance, 'The Chromosomes of the Chick Soma', *Biol. Bull.*, li, 1926, pp. 443–8.

germinal mitotic behavior and in consideration of the complete inability of highly specialized cells to regenerate other than cells similar to themselves, it is tentatively suggested as a basis for future discussion that the somatic chromosomes, as far at least as their genetic function is concerned, have either become functionless or their cytoplasmic environment is incapable of reacting to the possibilities presumably carried by them' (p. 446).

It would be more logical to conclude that the cause of cellular differentiation lay in the cytoplasm or more properly in the complete cell, in its relations to other cells and to the developing organism as a whole. The Morgan school, however, apparently still believe that the cytoplasm is of secondary importance,[1] and that it is controlled by the genes.[2]

While the theory of the gene in its present formulation has little significance for the major problems of heredity and development, dealing as it does in terms of abstract and hypothetical units, whose function it is to explain differences but not the ontogenetic process as a whole, there remains of course the possibility of a physiological or physico-chemical reinterpretation of the demonstrated facts which will throw light on the real functions of the chromosomes in general metabolism and development. That the chromosomes exert a powerful influence in modifying the course of development is already clear, and for this advance we have to thank the geneticists; it should not be long before some adequate physiological theory is formulated as to the way in which this influence is exerted. There are in fact not wanting signs that the gene theory is already in course of modification and, it may be, transformation. Something is already known of the actual chemical processes underlying the Mendelian inheritance of pigments, and the theory of genic balance[3]

[1] T. H. Morgan, 'Genetics and the Physiology of Development', *American Naturalist*, lx, 1926, pp. 489–515.

[2] Morgan, Bridges, and Sturtevant, 'The Genetics of *Drosophila*', *Bibliographia Genetica*, ii, 1925, p. 84. See also Morgan, *Experimental Embryology*, 1927, pp. 7–9, 208–9, and 654–5.

[3] 'Bridges' work on genic balance shows that the effect of a gene depends not only upon environmental conditions but also, and particularly, upon the other genes with which it is associated in the hereditary constitution of the individual', Crew, op. cit., p. 733.

appears to be a step in the direction of a more physiological interpretation of the gene hypothesis. To become really physiological, however, the theory must throw off all traces of the particulate conception of heredity; having already shaken off the idea of *representative* particles, it must go farther and get rid of hypothetical 'particles' altogether. We shall at a later stage (see Chapter XIV) take up this important question of the relation of the chromosomes to development, and attempt to fit in the genetic facts with an 'organismal' theory of development.[1]

To sum up with regard to the gene theory *in its original formulation*—we have seen that the theory is markedly inferior to Weismann's as an explanation of development, that, in fact, it is not really a theory of development at all. It gives a formal explanation, based upon the behaviour of the chromosomes and their presumed constituent elements, the genes, of certain rather superficial aspects of heredity, namely the laws of inheritance of such minor mutations as are not incompatible with fertile inter-crossing, but it has not as yet linked up its ultimate elements, the genes, in any understandable way with our present knowledge of the physiology of the cell and the organism. It can by its very nature offer no explanation of the spatial and temporal harmony of development, nor of recapitulation, and it ignores completely the historical aspect of development. There is observable indeed in the writings of the Morgan school a distinct tendency to deny the validity of many of the concepts regarding adaptation and evolution which are commonly accepted by biologists—presumably because such concepts cannot find a place in the genetic scheme.[2]

The methodological assumptions of the theory of the gene are very similar to those of Weismann's theory. There is the

[1] Our criticism of the gene theory, which may appear unnecessarily severe, is directed solely against its methodological assumptions. The value of the facts established by genetical research is not denied; the reader is referred to Chapter XIV (pp. 279–87) for an appreciation of the important part played by the chromosomes in development and heredity.

[2] On the relation of the gene theory to the problems of evolution and adaptation, see J. T. Cunningham, *Modern Biology*, London, 1928.

same deep-rooted conviction that heredity must be explained as due to the transmission of an unchanging *substance*, the germ-plasm, in accordance with the materialistic principles which are accepted as the only basis for a scientific biology.[1] Like Weismann's, the theory does not reach the stage of being stated in physico-chemical terms, but remains non-physiological and to a large extent abstract, though it is probably developing towards a more physiological formulation. Like Weismann's again, it postulates independent material determinant units, though the simple relation between determinant and determinate is gone. These units, the genes, are arrived at by a process of reification of differences, and are in fact quite as hypothetical as Weismann's determinants. Though the genes remain rather bare of qualities, as befits their function as symbols, it is assumed that they do in some way 'determine' the appearance of the characters of the organism. We shall consider this assumption more fully at a later stage.

[1] One of the leading exponents of the gene theory writes: '. . . the biological investigator, in wielding his formulae, should not remain content until the abstract "tendencies" or "concepts" he arrives at can be translated analytically into terms of the arrangements and methods of movements of concrete particles', H. J. Muller, *American Naturalist*, lxi, 1927, p. 416.

VI

SOME MODERN EPIGENETIC THEORIES

THE theories of the germ-plasm and the gene, and in fact all theories dealing in terms of hypothetical particles conditioning or determining development, belong, of course, to that same current of thought which produced the early theories of preformation. We have now to consider some modern epigenetic views, whose upholders naturally found themselves in more or less complete opposition to the modern preformationists, and we select as the main representative of this line of thought the distinguished French zoologist Yves Delage.

In his remarkable book on the major problems of biology[1] Delage gives a valuable historical account and critique of the main theories of development and heredity, particularly those of the nineteenth century, and indicates in broad outline a theory of his own which he calls the 'théorie des causes actuelles'.

He opposes vigorously the Weismannian conception that all the potentialities of the germ are already present therein in material form, and he rejects completely the notion of representative particles. It is not necessary to follow in any great detail his thoroughgoing criticism of the numerous 'micromeristic' or particulate theories, which he contrasts to their disadvantage with the 'organicist' views held by W. Roux and himself; we may, however, briefly consider his treatment of Weismann and H. de Vries. To the general hypothesis that there may exist ultra-microscopic particles, intermediate between cellular units and molecules, and capable of assimilation, growth, and division, he raises no objection in principle, but he points out the futility of assigning to such particles special powers of determining the course of development. If they are assumed to represent and

[1] *La Structure du Protoplasma et les Théories sur l'Hérédité et les grands Problèmes de la Biologie générale.* Paris, 1895, 2nd edit., 1903; quotations are from the first edition.

determine particular characters of the organism, two alternative logical possibilities arise. Either they represent the concrete characters of the organism, in which case their number must be infinite, or they represent abstract or subjective characters, in which case their own existence is equally abstract and subjective, i.e. they do not exist materially at all but are mere symbols. Weismann's system is one of complete preformation—all his Ids must have been present in the ancestral Protozoa—and it does not allow for the influence of environment and the new-creation of form. He has got all that can be got from the concept of representative particles; if his system is a failure it is because the fundamental hypothesis is false: 'Let us therefore draw the conclusion: there do not exist in the germ-plasm distinct particles representing the parts of the body or the characters and properties of the organism' (p. 719).

H. de Vries' theory of intra-cellular pangenesis (1889) has in some ways so close a resemblance to the gene theory that it is of much interest to consider Delage's criticism of it. De Vries held that the germ-plasm was present in the nucleus of every cell, germinal and somatic alike, and that cellular differentiation was due to the issuing out from the nucleus of particular kinds or groups of pangens which impressed upon the cytoplasm its special character. The theory is well summarized by Delage as follows:

> 'The elementary characters and properties of organisms have as factors material particles, the pangens, intermediate between chemical molecules and cells; the immense diversity of organisms is based on the almost infinite variety of possible combinations of the pangens; the pangens are contained in a latent state in the nucleus, which serves to transmit them to the fertilized egg in reproduction, and from cell to cell in ontogeny; finally these pangens issue from the nucleus and spread through the cytoplasm to which they impart its particular properties, and cellular differentiation results from the fact that each cytoplasm receives only those that it needs for its particular development and for the functions it is destined to fulfil' (p. 660).

Delage argues that the elementary characters which de Vries distinguishes are for the most part the product of subjective

selection by the observer, and that accordingly they cannot possibly be represented by material particles.

'De Vries reasons', he points out, 'as one who should say: copper has a certain density, it is malleable, capable of taking a polish, it is yellowish red in colour and gives out a particular smell when rubbed, it oxidizes in certain conditions, &c., &c. All these properties are independent, for we see them all varying independently of one another. Thus colour is independent of density, for gold is yellower and less red than copper, it is also heavier; and lead is also heavier, though it is neither yellow nor red. Density for its part is independent of hardness, for lead, though it is denser is yet softer, and tin, though less dense, is softer also, while iron and platinum, though one is less dense and the other more dense, are both harder. From which we can conclude that all these properties, density, colour, hardness, smell, &c., are independent and must be supported by independent material factors. Metals then are not simple bodies, they are formed of particles of which some supply colour, others density, others malleability and so on, and the different metals result from different mixtures of these elementary particles' (p. 662).

The analogy sounds a little far fetched, but, as we shall see later, it is from Delage's own point of view quite a fair analogy. He raises the further objection to de Vries' theory that it does not account for the activation at the proper time and place of the special sets of pangens responsible for cellular differentiation; since by hypothesis all the nuclei have the complete set of pangens, the stimulus to differentiation, to the issue of the right pangens from the nucleus, can only come from the cytoplasm. This is, of course, a difficulty which the gene theory also has to face (see above, p. 70).

Delage's own view of development and heredity may best be described as a theory of chemical epigenesis. His fundamental hypothesis is the mechanistic one that the structure of protoplasm is the mechanical cause of the phenomena of life. He holds that life is a resultant of the properties of living matter, and that these properties are the outcome of its physico-chemical constitution (p. 403). His theory is singularly free from speculation; it follows the facts closely, and is in effect a generalization of the observed data, con-

sidered from the physiological point of view. Therein lies its great value. Let us summarize its main outlines.

Protoplasm is a complex chemical mixture with, in addition, a certain structure. There is no reason to assume the existence of permanent vital units of a lower order than the cell. Nuclear division is always exactly quantitative and gives identical products; differentiation accordingly must be of cytoplasmic origin, for it is in their cytoplasm that two daughter cells first of all show differences, and if differences are later established in the nuclei, this can only come about subsequent to, and as a consequence of, the cytoplasmic differences (p. 759). The nucleus is thus not in any sense the dominating partner in the cell, as most other theories assume.

There is no rigid determination of characters in the egg. Differentiation in development depends to a large extent upon the relative position of the parts and upon environmental conditions. There is an actual new-formation of substances in ontogeny—a chemical epigenesis—and histological differentiation is in the main a consequence of this chemical differentiation. All development is based upon metabolic processes, and the nature of the food and of the products of dissimilation exerts a profound influence upon its course. The functional correlation of organs and cells is important. 'In sum, ontogeny is not merely the development, separation, and accentuation of tendencies completely represented in some form, material or other, in the fertilized egg. It is partly that, and partly a progressive formation of parts and of properties actually new, and the initial constitution of the egg is only one of the indispensable conditions for this formation' (p. 765).

Delage accepts in general the distinction between somatic and germinal cells, but does not regard it as absolute. For him the ovum is relatively simple in structure, essentially a slightly differentiated cell which has taken little or no part in somatic differentiation, and is thus capable of returning to its initial condition. The eggs of related species are much more alike than are the adults;[1] the egg does *not* contain all

[1] Contrast O. Hertwig's concept of the 'Species-Cell', *Allgemeine Biologie*, 6–7th edit., Jena, 1923, p. 492.

the elements of its development—the greater part it will find in the environment or make by the way. But while the egg has little or no preformed structure 'its physico-chemical constitution is extremely precise, and the least difference in this respect is necessarily amplified to considerable proportions in the course of ontogenetic differentiation, and may lead to the considerable differences which exist between adults arising from different eggs' (p. 772). Much of the apparent preformation is really environmental—to use a paradoxical expression. Since the egg is of precise and delicate organization it can develop only under very exactly delimited conditions.

'It is therefore held between these two alternatives—to find from moment to moment the exact conditions necessary to it, or to die. Therein lies the whole explanation of heredity. For these conditions are precisely those which the egg of the parent has encountered at each corresponding stage. It is therefore inevitable that it follow the same development as the egg of the parent, since it has the same physico-chemical constitution, and encounters, in the same order, a series of identical conditions which are rigorously determined. It is therefore not necessary that it should contain within itself all the factors of its development. It is sufficient that it contains *one* of the numerous factors indispensable to the identical reproduction of all the developmental phenomena, the other factors, no less indispensable, are situated outside of it, but the egg is certain to encounter them at the proper place and time, without which it dies, and development is not diverted but stops. To the inorganic object, the star or the river, there are open at every moment a thousand different ways which all lead to a normal goal; its development has nothing precise about it. To the organized being also many diverse paths are open every moment, but all lead to certain destruction, save one—that path which leads it to the goal its parents reached. Is it then necessary to suppose that it knows the way, or to be amazed that when it has succeeded in following a line right to the goal, this way has led it to the same goal its parents reached before it?' (p. 777).

The orderly progression of development, its repetition of the parental ontogeny, and its steady course towards an apparent end or goal, finds thus a simple explanation which is independent of any elaborate hypothesis of preformation in the egg.

As applied to ontogeny, the theory of representative

particles merely adds unnecessary complications to the simplicity of the facts. The fertilized ovum exercises certain simple vital functions; its descendants gradually acquire specialized functions, though no individual cell acquires any excessively complex or multiple functions. The cells therefore change in the course of ontogeny, but if one does not imagine them loaded with all the future properties of their descendant cells (as is done in the preformistic theories) there is no need to ascribe to them any excessively complicated structure. The fault of all preformistic and particulate theories is to translate these *future* possibilities of development into material predispositions—to hypostatize all potentialities as material actualities, preformed and held in reserve. But these 'potentialities' are purely virtual and conceptual—their appearance is entirely dependent upon future environmental conditions. 'Latent' characters of this kind are accordingly purely conceptual and do not actually exist. 'It is the erroneous idea that the properties of the daughter-cell, and in consequence the physico-chemical aggregate which is the basis of these properties, must be found already formed in the mother-cell, that has led to the forging of so many hypotheses, as useless as they are improbable, about the structure of the idioplasm' (p. 779).

The egg, therefore, regarded as it is and without hypothesis, has only the characters of the moment, and does not already possess those of its descendant cells; there is accordingly in each ontogeny a real formation of characters not originally present in the egg.

'*Latent or potential characters are absent characters.* . . . The egg contains nothing beyond the special physico-chemical constitution that confers upon it its individual properties *qua* cell. It is evident that this constitution is the condition of future characters, but this condition is in the egg extremely incomplete, and to say that it is complete but latent is to falsify the state of affairs. What is lacking to complete the conditions does not exist in the egg in a state of inhibition, but outside the egg altogether, and can equally well occur or not occur at the required moment' (p. 781). Ontogeny is *not* completely determined in the egg.

In effect, Delage rejects the idea of germinal *substance*; he states his theory throughout in terms of cells, regarded as physico-chemical systems.

A further important consequence of this objective, physiological interpretation of the constitution of the egg-cell is the rejection of the preformistic notion of a point-to-point correspondence between the structure of the germ-plasm and the structure or properties of the adult organism. From this point of view there is absolutely no foundation for the theory of representative particles. 'From the physico-chemical structure [of the cell] result properties and characters which cannot help expressing themselves, and are, *taken together*, the result of the *totality* of this structure' (p. 782).[1]

This general determination of properties is not peculiar to organic systems; the totality of properties belongs to the totality of the aggregate in chemical compounds as well.[2]

It is quite possible, he argues, to harmonize this view of *general* determination with the undoubted fact that special peculiarities may be transmitted apparently as units. A slight modification of the germ-plasm may result in a specific and definite change in the adult organism, and may accordingly recur in future generations, but the modification itself is not necessarily particulate and localized; it must, from the physiological point of view, be regarded as a slight but definite change affecting the physico-chemical system of the germ-plasm or egg-cell as a *whole*.

When, for instance, two allied forms differ in some special characters their germ-plasms are extremely similar, but there must exist nevertheless a very slight difference of physico-chemical constitution between the two germ-plasms *affecting the whole* and not merely the particular parts specially related to the characters in question.

In sum,

'All the parts of the egg . . . including the ultramicroscopic parts

[1] 'De cette structure physico-chimique résultent des propriétés et caractères qui ne peuvent pas ne pas s'exprimer, et qui sont *tous ensemble* le résultat de *l'ensemble* de la structure.'

[2] Cf. his argument concerning the properties of metals (*supra*, p. 78).

whatever they may be, correspond *all and each* to the totality of the organism. Certain chemical substances may have a special affectation or a localized destiny, but there is no representation of the parts or the characters of the organism by an equivalent number of special particles in the egg, having relations only with these, and remaining latent up to the moment when they arrive in the cells in which they are due to become active. It is therefore a matter of indifference whether the initial peculiarity affects the whole egg-cell or merely one of its parts, it will affect none the less the organism as a whole' (p. 786).

It is interesting to see how in this brilliant analysis Delage arrives by mere dint of clear thinking at the result laboriously worked out by the Morgan school that each gene acts to some extent upon all characters. Delage took the further logical step that representative particles are superfluous abstractions, and the same conclusion applies equally to genes, in so far as they are regarded as independent and particulate units. Even had Delage known of the factorial basis for the gene theory he would not have required to modify his essential argument. If certain characters are actually 'carried' by certain parts of the cell, to wit, the chromosomes, these parts are still constituent elements of the physico-chemical system of the cell as a whole, and cannot be treated in isolation from the rest of the cell. Delage's argument thus includes and allows for this special case.

Delage's criticism of particulate theories is in fact unanswerable. If the cell and the developing organism are regarded as physico-chemical systems in constant metabolic relations with their environment, external and internal, there is absolutely no place for independent and isolated material units which represent or determine certain characters or groups of characters. No part of the cell can exist in isolation from the whole; to imagine such is to create a conceptual fiction to which nothing corresponds in reality. To ascribe determinative, as distinct from conditioning, powers to such fictive units is unscientific and explains nothing. As a purely provisional concept, the gene may have some practical utility, provided its fictitious nature be kept clearly in mind, but, as we have seen, it is doomed to be superseded

as soon as the physiological interpretation is discovered of the facts on which the hypothesis is based.

It is not necessary to follow out Delage's general views on development, heredity, and evolution in further detail. He exhibits throughout a clarity of thought, fidelity to the facts of observation, and a sobriety of hypothesis that make his book one of the finest contributions to general biology ever written.

The physiological point of view is put very clearly also by Verworn,[1] who goes even farther than Delage in his rejection of preformistic doctrines. He points out that heredity and development are essentially phenomena of cells and organisms, and cannot be interpreted in terms merely of hereditary substance. They must be stated in terms of metabolism, for development and reproduction are an expression of changes in the metabolic relations between cell and medium, conditioned by growth, and growth is the cause of all development, both of the individual cell and of the whole cell-community. Like Delage he denies the necessity for assuming in the egg-cell an elaborate and complex organization; it is incorrect, he says, 'from the fact that the small egg is differentiated into a cell-structure of astonishing complexity, to deduce the idea that the living substance of the former in comparison with that of every other cell, either every unicellular organism or every tissue-cell, must be distinguished by an inconceivably delicate and complex structure' (p. 537).

The problem of hereditary transmission is met with in its simplest form in unicellular organisms.

'It is seen here that the transference of the characteristics of the ancestors to the descendants, takes place by the transference of substance which possesses the characteristics of the ancestors. In order that this substance may possess all the characteristics of the latter, it must be a complete cell with all the essential cell-constituents. The characteristic peculiarities of the mother-cell are the expression of its metabolism. If, therefore, the peculiarities of the mother-cell

[1] Max Verworn, *Allgemeine Physiologie* (1895, 7th edit., 1922) English Translation, as *General Physiology*, London, 1899.

are to be transmitted to the daughter-cells, its whole metabolism must be transmitted. But this is possible only when a certain quantity of all the essential constituents, i.e., of the protoplasm and nucleus of the mother-cell, passes over to the daughter-cell, for otherwise the metabolism of the latter would not be able to continue, and the cell would necessarily perish. In fact, it is seen not only in unicellular organisms, but everywhere in organic nature, that hereditary transmission takes place without exception by means of the transference of a complete cell with nucleus and protoplasm' (pp. 544–5).

The physiologist does not take kindly to the idea of a *hereditary substance* localized somewhere in the cell and transmitted intact in reproduction, for a substance that is to transmit the characteristics of a cell to its descendants must itself be alive. It must accordingly have a metabolism, and this is dependent upon its relations with all the other substances necessary to cell-metabolism, dependent, that is, upon the integrity of *all* the essential constituents of the cell. The singling out of a *single* cell-constituent as the special bearer of heredity is wholly unjustified; the cytoplasm is of equal value in this respect to the nucleus, and hereditary transmission is invariably mediated by the germ-cell as a whole.

The real vital unit is in fact the individual cell: 'if the conception of the organic individual is not to be given up, it must be regarded as an unconditional requirement that the organism be characterized by the presence of all those vital phenomena that have to do with self-preservation. Only the cell fulfils this condition; it is, therefore, the individual of the lowest order and the elementary organism' (p. 64).

Verworn, it is true, elaborated a hypothesis that living substance was composed of biogens or elementary units possessing the metabolic characteristics of life, but the merit remains his of emphasizing the fact that life itself and the hereditary potentialities can be handed on only by the cell as a whole. It is the cell and not the germ-plasm that guards and transmits the flame of life—*lampada vitai tradit.*

The concept of individuality is, as we shall see later, of prime importance for biology. Verworn thought of the

organic individual as a physico-chemical system; E. G. Conklin in his admirable lectures[1] goes one step farther and associates both the physical and the psychical attributes of life in the common concept of organization. He considers that 'the body or brain is not the cause of mind, nor mind the cause of body or brain, but that both are inherent in one common organization or individuality' (p. 49). This applies also to the germ: 'In the simplest protoplasm we find organization, that is, structure and function, and in germinal protoplasm we find the elements of the mind as well as of the body, and the problem of the ultimate relation of the two is the same whether we consider the organism in its germinal or in its adult stage' (p. 50). Organization then at all stages includes both structure and function, mind and body, and continuity of organization implies not only persistence of structure but persistence of function. 'Indeed the entire organism, structure, and function, body and mind, is a unity, and the only justification for dealing with these constituents of the organism as if they were separate entities, whether they be regarded in their adult condition or in the course of their development, is to be found in the increased convenience and effectiveness of such separate treatment' (p. 81).

Conklin in his treatment of the facts of development lays stress upon the evolution of function, and adopts essentially the same view as Delage—that development is an epigenesis, predominantly chemical, leading to an actual new-formation of structure and function.

'Development is not the unfolding of an infolded organism, nor the mere sorting of materials already present in the germ-cells, though this does take place, but rather it consists in the formation of new materials and qualities, of new structures and functions—by the combination and interaction of the germinal elements present in the oosperm. In similar manner the combination and interaction of chemical elements yield new substances and qualities which are not to be observed in the elements themselves. Such new substances and qualities, whether in the organic or in the inorganic world, do not

[1] E. G. Conklin, *Heredity and Environment in the Development of Men*, 2nd edit., Princeton, 1916.

arise by the gradual unfolding of what was present from the beginning, but they are produced by a process of "creative synthesis" ' (pp. 88–9). There is thus both in development and in cosmic evolution a real formation of new qualities, a real 'emergence' as Lloyd Morgan would say.

His own researches had shown him the importance of cytoplasmic differentiation in the egg, and he concluded that the hereditary potencies of the male and female germ-cells were not equal—that 'the polarity, symmetry, type of cleavage, and the pattern, or relative positions and proportions of future organs, [are] foreshadowed in the cytoplasm of the egg cell, while only the differentiations of later development are influenced by the sperm. In short the egg cytoplasm fixes the general type of development and the sperm and egg nuclei supply only the details' (p. 184). The chromosomes are certainly important, but in no case can the cytoplasm be regarded as merely serving as food or environment for the chromosomes. It is the entire cell, both nucleus and cytoplasm, that is concerned in heredity and differentiation.

In his book *The Organism as a Whole*[1] that redoubtable protagonist of the mechanistic point of view, Jacques Loeb, tackles the problem of the harmony and co-ordination of the living things, and expresses his dissatisfaction with the particularist conception revived by the researches of the Morgan school. He admits the importance of this problem, which, as he says, has always raised doubts as to the adequacy of the physico-chemical point of view.

'The difficulties besetting the biologist in this problem have been rather increased than diminished by the discovery of Mendelian heredity, according to which each character is transmitted independently of any other character. Since the number of Mendelian characters in each organism is large, the possibility must be faced that the organism is merely a mosaic of independent hereditary characters. If this be the case the question arises: What moulds these independent characters into a harmonious whole' (p. v).

[1] *The Organism as a Whole, from a Physicochemical Viewpoint.* New York and London, 1916.

The solution put forward by Loeb is that the unity of the organism is present from the beginning in the structure of the egg, particularly of its cytoplasm. The egg is the embryo in the rough, and the Mendelian factors in the chromosomes add only the finishing touches, probably by giving rise to special hormones and enzymes. Genus and species heredity would on this conception be determined by the cytoplasm of the egg, and would in the long run be dependent upon the chemical specificity of the proteins.

We shall at a later stage in this book come back to Loeb's theory of the 'embryo in the rough'; meanwhile, for our present purpose, the main point is his criticism of the particularist point of view, and his substitution for this of the conception of the organism as a harmonious physico-chemical system. His treatment of development is biochemical—it is a question, he holds, of the mechanism by which the 'non-specific building stones' in the food are synthesized into the specific proteins of the species (p. 28). This purely biochemical point of view is very clearly put by R. S. Lillie,[1] who also emphasizes the importance of the specificity of the proteins. The following quotations give a good idea of his standpoint.

'The problem of heredity is not a problem to be dealt with by itself; it becomes identical with the most fundamental problem of general physiology, the problem of how living protoplasm is synthesized from non-living matter' (p. 70).

'It is not a coincidence that living organisms, the most complex systems, in the structural sense, occurring in nature, are also the most complex in the purely chemical sense; and all of the evidence indicates that the structural complexity is the expression or consequence of the chemical complexity. The essential reason for this appears to be that a high degree of chemical specificity or individualization is the necessary prerequisite for structural complexity, and that chemical specificity depends largely upon peculiarities of stereochemical configuration. The number of individualized isomers in the case of any organic compound increases rapidly with increase in the number of asymmetric carbon atoms in the molecule. Hence the proteins,

[1] R. S. Lillie, 'Heredity from the Physico-Chemical Point of View', *Biol. Bull.* xxxiv, 1918, pp. 65–90.

formed of linked amino-acids, most of which are asymmetric compounds, exhibit the possibilities of chemical individualization to a greater degree than any other known class of compounds. It is further significant that proteins which are specifically distinct chemically, although otherwise closely similar—e.g. haemoglobins from different species—tend to form crystals, i.e., structural aggregates, which are specifically distinct in their form-characters' (pp. 72–3).

Chemical specificity is the basis of morphological and physiological specificity,

'and chemical specificity is primarily the property of the proteins. Other biochemical compounds appear to be chemically the same wherever found, but the proteins vary in their specific character from species to species. Moreover, physiologically corresponding or "homologous" proteins are more nearly alike in their chemical and physical characters the more closely related the species are from which they are taken. There is thus a general parallelism between the degree of chemical relationship exhibited by homologous proteins from different organisms, and the degree of biological relationship existing between the species' (p. 74).

The chromosome theory does not fare very well at the hands of the biochemist, who fails to find any chemical basis in the chromosomes for the extreme complexity of structure required by the theory. This is clearly brought out by A. P. Mathews,[1] who writes:

'The structure which the cytologist calls a chromosome and in which most see the bearer of all the hereditary traits and some even go so far as to imagine that each trait or character is represented by a distinct unit or gene, this structure as shewn in the fixed dyed section is nothing else than a salt of nucleic acid with the basic dye which has been used to stain it. Whether in addition to the dye there is present also some protein matter cannot be definitely stated' (p. 75).

Our knowledge of the composition of chromatin lends no support to the hypothesis that the chromosomes are of highly complex structure. Where in theory we should expect to find the most complex compounds, e.g. in the sperm head, we find the simplest.

'Our ignorance of the chemistry of all these complex compounds,

[1] In E. V. Cowdry, *General Cytology*, Chicago, 1924.

however, is still so great that no chemist would be willing to make the affirmation that the chemical facts conclusively disprove the chromosomal theory of inheritance. At the best, or worst, they give little if any support to this view. In the author's opinion, which is here given for what it is worth, the chromatin of spermatozoa is nothing else than the chromatin of spermatozoa: and that of an egg cell is the chromatin of an egg cell. They are not nerve, muscle, epithelial chromatin, in masquerade. While when united they may lead to the formation of all the other chromatins of the body, or at least play an important part in their formation, neither should be regarded as a museum containing samples of all the different products which it is capable of making. For since the number of these products is in fact infinite for each chromatin, as is shewn by the differences in cells produced by any change in the conditions of development, by the accidents of existence, such as galls on plants, &c., there is not room in the chromosomes for all these samples. But if the chromatin can make some other chromatins without having a sample to guide it, why not make them all? Why have any samples at all? Considerations of this nature will have different weight with different minds. And it must be remembered that the onus of proof is on those who assert that the chromosomes are such museums containing samples of all the chromatin of all the cells of the body, not only all the chromatins which develop during life, but all that infinite collection of old masters inherited from the past and all the infinite number of descendants yet to appear in the eons before us, and presenting qualities usually said to be dormant. They are concealed no doubt in the chromosomal attic, ready to be produced when occasion arises' (p. 90).

It would be easy to give many other examples of the modern physico-chemical or physiological treatment of the problems of development; we shall conclude however with a brief reference to certain general views expressed by C. M. Child[1] which are based on a life-long study of regeneration and regulation. In his book on *Individuality in Organisms*, Child tackles the problem of unity and co-ordination which constitutes such a difficulty for all particulate theories of development. Though remaining a mechanist, he works out a dynamical and functional conception of the organism and its

[1] *Individuality in Organisms*, Chicago, 1915. See also *Senescence and Rejuvenescence*, Chicago, 1915.

development which is a distinct advance upon the ordinary static 'machine-theory'. Most theories assume an 'organization' of some kind or other as a starting-point; Child points out that the real problem is the way in which this organization is formed, and he attempts to show how the primary organization of the embryo may arise epigenetically through graded differences in metabolic rate along the primary axes. Theories of representative particles, theories of organic crystals, theories of a pre-established physico-chemical unity, all 'proceed on the conception that a certain more or less complex "organization" is necessary as a starting-point; the machine must somehow be constructed before it can run' (p. 25). But 'to believe that metabolism results from structure and "organization", as the activity of the man-made machine results from its structure, is to ignore the fact that metabolism is the formative agent in the organism' (p. 25). The static view of the organism ignores the fact that 'life is function. In no case does the organism begin to function only after its construction is completed; it always functions from the beginning; it constructs itself by functioning, and the character of its functional activity changes as its structural development progresses. Structure and function are mutually related. Function produces structure, and structure modifies and determines the character of function' (p. 16). What we see as protoplasm and structure is to be regarded not as the *cause* of metabolism and vital activity but as the relatively stable *results* of functional activity. (Cf. Roux, p. 104 below.)

Child's own solution of the problem of unity is, in outline, as follows:

'The organic individual, as a living entity possessing some degree of physiological—not merely physical—unity and order, consists in its simplest forms of one or more gradients in part of a cell, a cell, or a cell-mass of specific physico-chemical constitution. The process of individuation is the process of establishment of the gradient or gradients as a more or less persistent condition, and the degree of individuation depends upon the permanency of the gradient, the metabolic rate in the dominant region, the conductivity of the protoplasm, and probably on other factors as well. From this point of view

the assumption of a mysterious, self-determined organization in the protoplasm, the cell or the cell-mass as the basis of physiological individuality becomes entirely unnecessary. The origin of physiological individuality is to be found, not in living protoplasm alone, but in the relations between living protoplasm and the external world' (pp. 40–1).

It will be seen that Child's position may best be described as a dynamical epigenesis. In this dynamical conception of the organism, the starting-point of ontogeny lies not in a certain organization but in a certain reaction-system. It is this reaction-system which constitutes the basis of existence, and it is in this system that differences in metabolic rate initiate the process of differentiation (p. 188). The organism acts as a unit in inheritance and development; it is incorrect to treat of these phenomena in terms of germinal *substance*, or even of cells, or in terms of any form of pre-existing organization.

'If the organism is fundamentally a specific reaction system in which quantitative differences initiate physiological individuation, development and differentiation, nothing can be more certain than that it acts essentially as a unit in inheritance. It is the fundamental reaction system which is inherited, not a multitude of distinct, qualitatively different substances or other entities with a definite spatial localization. Development is not a distribution of the different qualities to different regions, but simply the realization of possibilities, of capacities of the reaction system. The process of realization differs in different regions because the conditions are different. Neither characters nor factors as distinct entities are inherited, but rather possibilities, which are given in the physico-chemical constitution of the fundamental reaction system, but not necessarily localized in this or that part of it' (p. 202).

Child's dynamical and functional point of view enables him to shake free from the germ-plasm hypothesis altogether, with its absolute separation of soma and germ-plasm, and gives at least the possibility of a rational treatment of the problem of the transmission of acquired characters and the utilization of the mnemic conception (pp. 203–4). His criticism of the particulate theories of heredity is outspoken and pertinent, and we cannot resist a last quotation.

'These theories postulate in one form or another a multitude of specific material entities, each of which represents in some way some characteristic of the organism. The organism as we know it is the product of their combined and harmonious activity. Examination of these theories shows that these hypothetical entities, gemmules, determinants, physiological units, pangenes, specific accumulators, or whatever we prefer to call them, are themselves endowed, *ex hypothesi*, with the essential characteristics of individuals, and that the organism as a whole is merely a composite of their orderly activities. Neither the problem of the individuality of the hypothetical units nor that of their orderly combination and unification in the organism receives any adequate consideration in those theories. They merely translate the problem into hypothetical terms which are beyond the reach of scientific method. The combination of these units into the individual is assumed to occur as the facts demand, and although the problem of the control and ordering of such units through all the changes involved in the development of a complex organism, say the human being, is one which staggers human intelligence, it is practically ignored' (pp. 22–3).

Essentially the criticism that Aristotle made of the Hippocratic doctrine of pangenesis! Child has fully appreciated the importance of the problem of 'composition'.

Our survey of modern epigenetic theories, which are based for the most part upon a physico-chemical or physiological treatment of the problems of development, has necessarily been somewhat slight and superficial. Certain points nevertheless emerge with sufficient clearness. These theories represent a very healthy reaction from the static, morphological, particulate conceptions of the modern preformationists. They keep much closer to the facts of observation, and the purely speculative element in them is less prominent. They represent generalizations of fact rather than hypothetical constructions. They give full weight to functional activity and the influence of environment, and avoid the sterile view that all is predetermined in the egg, in some mysterious germinal *substance*. Several emphasize the importance of considering the cell as a whole in development and heredity.

The even more significant conception of the organism

itself as a functional whole, in which no part or process can be properly understood in isolation from the activity of the whole, begins to emerge in these theories—whether in the form of a physico-chemical *system*, or in the more subtle but more accurate form of a dynamical or metabolic unity, as in the theories of Child. Conklin gives clear indication of a comprehensive conception of organization, which shall include both the structural and the functional, the physical and the psychical, aspect of living things.

VII

WILHELM ROUX AND THE MECHANICS OF DEVELOPMENT

THE experimental study of development arose almost contemporaneously with the cytological studies that culminated in the theory of the germ-plasm, and it owed more to William Roux than to any other man. But one forerunner, W. His, deserves passing mention. In 1874,[1] in revolt against the prevailing fashion of phylogenetic speculation, he pointed out that the problems of development were essentially physiological, and he went some way towards indicating the proper line of attack upon them. His principle, for instance, of organ-forming areas in the germ[2] was later to prove a valuable and important one, and his 'principle of unequal growth' was also fertile.

His attitude was that of the physiologists of his time who based their work on the mechanistic hypothesis. Each stage of development was regarded by His as the sufficient cause of the next, which followed mechanically from it, and it was the business of embryology to trace out these causal connexions.

'Embryology', he wrote, 'is, in essence, a physiological science; it has not only to describe the building up of every single form from the egg, according to its different phases, but to trace it back in such a way that every stage of development with all its peculiarities appears as the necessary result of those immediately preceding' (p. 2). Note the contrast with Baer's view (*supra*, p. 35) that each stage *conditions* the next stage in development, but is not in any full sense its cause.

[1] W. His, *Unsere Körperform und das physiologische Problem ihrer Entstehung*, Leipzig, 1874.

[2] 'I call *principle of organ-forming germinal areas* the principle according to which the germinal disc contains the plan of the organs laid out in superficial extension, each point of the germinal disc corresponding to one of the later developed organs' (p. 19).

His was a bitter opponent of Haeckel's 'biogenetic law' of recapitulation, and made the interesting suggestion, later developed by O. Hertwig,[1] that many of the early and simple stages of ontogeny are necessary results of the progress from simplicity to complexity, and may be explained without reference to ancestral history (p. 210). In general he accepted Baer's law of development, but emphasized the fact that specific distinctions are often observable in the very early stages of ontogeny.

Although there were experimentalists before Roux who tackled the problems of form, he may be regarded as the real founder of causal morphology, by reason of his pioneer work on functional adaptation and experimental embryology, his foundation of the *Archiv für Entwickelungsmechanik* (1895), the immense amount of research which he stimulated, and the hard thinking he put into the interpretation of his results.[2] For our special purpose here, the study of method, he is particularly important, in that he attempted to steer a middle course between a 'too simple' materialism and a 'metaphysical' vitalism—Scylla and Charybdis as he calls them in his Introduction to the *Archiv*—though remaining fully convinced that materialism formed the only sound basis for exact science.

We may consider first this introductory paper,[3] in which perhaps the clearest account of Roux's conception of biological method is to be found. The choice of the word *Entwickelungsmechanik*—the mechanics of development—is deliberate and significant. With Kant and Spinoza he considers that for the purpose of exact science causality is synonymous with mechanical necessity. Hence all science is in the long run mechanics, and the science of the production

[1] *Handbuch vergl. exper. Entwickelungslehre der Wirbeltiere*, iii, 3, pp. 149–80, Jena, 1906.

[2] The early history and development of causal morphology is outlined in *Form and Function* (1916), Ch. XVIII, where also many details of Roux's work are given which need not be reproduced here.

[3] 'Einleitung'. *Archiv für Entwickelungsmechanik*, i, 1895, pp. 1–41. English translation by W. M. Wheeler under the title 'The Problems, Methods and Scope of Developmental Mechanics' in *Wood's Holl Biol. Lectures for 1894*, Boston, 1895, pp. 149–90.

of form is properly designated the mechanics of development. Physics and chemistry attempt to reduce the most diverse phenomena to movements of matter; developmental mechanics must in the measure open to it attempt the same reduction. It need not push its analysis below the level of physico-chemical processes, and it may not at present be able to get even so far. This reduction to physico-chemical processes—to 'simple components' as Roux calls them—must, however, remain its ultimate aim.

But in practice we find that 'organic structure is mainly due to the operation of components which at present are so complicated as to exceed the limits of our observation'. These Roux calls 'complex components'. Although they depend in the last analysis upon simple components, 'nevertheless the complexity of their composition lends them attributes which often differ so widely from those of inorganic *modi operandi* ('Wirkungsweise') that they are not only very dissimilar but even appear to contradict in part the functions of these same inorganic *modi operandi* [simple components]' (Wheeler's trans., p. 153). The proximate task of developmental mechanics must be then to analyse the process of form-production into its complex components. These complex components may be mysterious in the sense that they cannot yet be fully explained in terms of their simple components, but in so far as they are constant and produce the same result under the same conditions they are of great scientific value in explaining development.

The complex components which Roux distinguishes are, first, the elementary cell-functions—assimilation, dissimilation, movement, division (as a special case of movement). To these must be added the more complicated functions of the cell, such as its powers of typical form-production and of qualitative self-differentiation. Underlying them all is the fundamental power of self-regulation without which living organisms could not persist. If we take into account the phylogenetic history of living things we must provisionally recognize still more complicated components, such as variation (adaptation) and heredity.

The result of such analysis applied to the development of any complicated organism is that

'all the extremely diverse structures of multicellular organisms may be traced back to the few *modi operandi* of cell-growth, of cell-evanescence (Zellenschwund), cell-division, cell-migration, active cell-formation, cell-elimination, and the qualitative metamorphosis of cells; certainly, in appearance at least, a very simple derivation. But the infinitely more difficult problem remains not only to ascertain the special role which each of these processes performs in the individual structure, but also to decompose these complex components themselves into more and more subordinate components' (p. 152).

It will be noticed that the method is purely analytical, and that its first result, as Roux himself admits, is complication rather than simplification. Simplification will only appear after analysis has been applied to many complex processes and has disclosed again and again the same simple components. There is no real attempt made towards a re-synthesis of the components distinguished; the concept of the organism as a unitary functional whole is disregarded by Roux; the complex components which his analysis disentangles are not joined up again and combined into the individualized activity of the whole from which by abstraction they were originally separated out.

Leaving this question of the unitary conception of the organism for further discussion later, we may note as characteristic of Roux's point of view that he considers the first business of developmental mechanics to be the discovery of the complex components of form-production and form-maintenance—the analysis of these into their simple components can wait. 'Developmental mechanics should', he writes, 'cultivate the analysis of formative processes into constant "complex components" to a greater extent, if anything, than the ascertainment of simple components' (p. 170). We must be content for many years to come with an analysis into complex components. Here then is the point of Roux's remark about Scylla and Charybdis to which reference was made at the beginning of the chapter. We may quote the passage in full:

'"*Incidit in Scyllam, qui vult vitare Charybdim*" is particularly

applicable to the investigator in the field of developmental mechanics. The *too simply mechanical* and the *metaphysical conception* represent the Scylla and the Charybdis, to steer one's course between which is indeed a difficult task, a task which few have hitherto accomplished. It cannot, however, be denied that the seductiveness of the latter views has been increasing with the increase in our knowledge' (p. 172).

Roux was no crude and unthinking materialist. While he accepted with full conviction the view that all material happenings, including the phenomena of organic development and activity, were mechanically determined and were in ultimate resort to be explained in terms of matter in motion, he was by no means blind to the complexity and mystery of organic activities, and he saw clearly that the reduction of life to ultimate mechanism was a goal so remote as to be almost unattainable; meanwhile the sound line of advance was to analyse the complex phenomena of life into simpler, more elementary functions, common to the majority of cells, tissues, and organs. He rejected dualistic vitalism on the ground that it inhibited research, by its insistence on the hopelessness of the task of arriving at a mechanistic explanation of life. He preferred to continue the struggle towards a possibly unattainable ideal.

His attitude to the vitalism of Driesch and others is clearly expressed in an important paper[1] written towards the close of his life, in which he looks back upon his life-work in the field of biological method. It is worth our while to reproduce the general argument of this paper, at least in outline, for the light it throws upon Roux's final position.

Living things, he declares, can be defined only in terms of function,[2] and he distinguishes nine fundamental properties or functions essential to life. These are much the

[1] 'Die Selbstregulation, ein characteristisches und nicht notwendig vitalistisches Vermögen aller Lebewesen'. *Nova Acta. Abh. K. Leop.-Carol. Deutschen Akad. Naturf.*, vol. c, Nr. 2, Halle, 1914, 91 pp. (The complete volume is dated 1915).

[2] See also his book *Die Entwickelungsmechanik, ein neuer Zweig der biologischen Wissenschaft*, Vorträge und Aufsätze über Entwickelungsmechanik, Heft i, Leipzig, 1905, where he states the 'functional minimum-definition' of life—'Living beings are bodies which change through causes inherent in themselves, but—also through inherent causes—have the power of remaining for a certain time relatively unaltered in spite of interchange of matter with the external environment' (p. 107).

same as he enumerated in his paper of 1895 (see above, p. 97) as 'complex components'. Abstraction is made of all psychical qualities of living things, though the existence and purposive nature of such qualities is not denied. To the nine functional properties there must be added one fundamental faculty before the definition is complete; this is the power of self-regulation, which is shown in the exercise of the nine main functions. 'From this general faculty there results direct adaptability to the change of external relations, as also protection against the effects of this change, and at the same time the power of self-maintenance and the stability of the organism are greatly increased' (p. 86).

Living things carry to a very marked degree the causes of their activity and development within themselves. For this reason Roux speaks always of the 'self-activity' of the organism and qualifies all the nine functions with the prefix 'Self'. This independence of environment is of course not an absolute one, but for the most part the environment supplies not the determining but the conditioning factors of organic activity. The main causes of form-production are to be sought inside, not outside, the organism.

The possession of these functional activities, together with the fundamental power of self-regulation, and the fact that these properties are 'self-determined', owing little or nothing of their essential nature and mode of manifestation to the external environment, mark off living things as in some measure different from all inorganic objects. 'The "totality" of these characteristic vital functions (*Autoergasien*) makes the living being into something different from all inorganic bodies, and invests it with a so-called inwardness (*Innerlichkeit*)' (p. 11). This is one of the passages in which Roux gets nearest to accepting the functional unity of the organism as something distinguishing it from all other material bodies (see also below, p. 105). The power of self-regulation, he admits, looks very much as if it depended upon a purposive agent, as the vitalists contend; but this power, as well as the other vital functions, might conceivably have arisen at the very dawn of life by selection of fortuitous variations

(p. 88)[1] and thus be in principle mechanically explicable. He concludes therefore that there is no proof that a mechanistic explanation of these specifically vital activities is impossible (p. 87). Hence we should reject vitalism, and continue to work steadily and doggedly along mechanistic lines.

He considers in some detail Driesch's supposed 'proofs' of the autonomy of vital processes and criticizes them acutely. Of very special methodological interest is the alternative hypothesis to Driesch's entelechy which he adopts as an explanation of the differentiation and regulation of structure in development. Driesch had objected that a complex machine-structure cannot possibly be divided in such a way that two replicas of half-size are formed, and yet on mechanistic principles this is what must happen at every cell-division throughout the course of development. Roux's reply is worth quoting at some length:

'A self-propagation of the "developed living creature", i.e. of a complete machine ready to function as such, does not take place at all in sexual propagation. But the "generative germ-plasm" proliferates, and from it there develops subsequently the new being. Who, however, in the present state of biology would maintain that this development took place therefore without the determining co-operation of the germ-plasm, in this case the somatic germ-plasm? In any case it is simpler to bring in the germ-plasm—the substance generally responsible for reproduction and heredity—rather than an entelechy. The actual reproduction as such of a machine, constructed for a specific purpose, need not be considered, since a specific reproductive substance contained therein, though not concerned with the actual functioning of the machine, can produce and further this reproduction. Reproduction can accordingly take place everywhere, corresponding to Weismann's continuity of the germ-plasm, by means of a substance evolved solely for this object, and adapted to it—the germ-plasm. The real problem of the reproduction of living things depends actually only upon the morphological assimilation of the germ-plasm. But that this substance produces that for which and through which

[1] In his voluminous writings and in particular in his early work *Der Kampf der Theile im Organismus* (Leipzig, 1881). Roux devotes much space to showing the possibility of the 'natural' origin of the fundamental vital functions. See also below, p. 103.

it has been evolved is not metaphysical, and requires no entelechy' (pp. 68–9).

It will be remembered how in discussing Weismann's theory we remarked that the germ-plasm played as it were the part of a 'materialistic entelechy' (see above, p. 50). Here we see that Roux actually puts in place of Driesch's entelechy the concept of an active form-producing germ-plasm. The one explanation is in fact the equivalent of the other. This point is a very important one for an understanding of the modern attitude towards the problems of development and heredity, and it will occupy our attention again in a later chapter.

It leads us also to consider some further aspects of Roux's conception of development, upon which we have not hitherto touched. Roux was a firm adherent of the germ-plasm doctrine, though not in the elaborate form given to it by Weismann.[1] He expressed it much more in physiological than in morphological terms. Thus he attributed to the germ-plasm a high power of self-regulation, to which its constancy from generation to generation was due. 'The constancy of the species is merely the ultimate product of the self-regulating mechanism of the germ-plasm, acquired only very slowly, but finally brought to a wonderful state of perfection. Thus in spite of great changes in the needs of its life externally, it remains relatively unchanged and propagates' (p. 38). Differentiation he considered to be due to the interaction of the germ-plasm of the somatic cells with the cell-body, and as early as 1903 he suggested that the cytoplasm acts as an activating and differentiating influence upon the uniform nuclear germ-plasm (p. 42, f. n.).

But speaking generally, the germ-plasm theory plays no very great part in what is distinctive in his thought. It is worth noting, however, that like most upholders of the germ-plasm doctrine he postulated the existence of ultra-microscopic units, after the fashion of Weismann's biophors,

[1] He was doubtful whether it was necessary to ascribe to the egg a highly complex germinal structure, and he believed much more in epigenesis than did Weismann (1905, pp. 101–3).

accepting thus the principle of 'biological atomism'. It is not necessary to enter into detail regarding the hierarchy of units which he distinguished[1]—isoplassons, autokineons, automerizons, idioplassons, and cell-organs—but one point may be brought out. The lowest conceivable unit is the isoplasson which exhibits metabolism, but need not have any elaborate morphological structure, for a flame, as Roux points out, also shows metabolism. An autokineon is an isoplasson possessing the faculty of movement. A certain degree of self-regulation characterizes both the isoplasson and autokineon, which may be regarded as phylogenetically the precursors of living beings, but not as being themselves possessed of the full qualities or properties of life. True living beings of the lowest order are the automerizons, which have the power of self-division. They are more or less equivalent to Weismann's biophors, de Vries' pangens, and other hypothetical units (1905, p. 115). A higher step is represented by the idioplassons, which have a definite morphological structure handed down by division. They appear to correspond with Weismann's determinants. At this stage there appears the all-important faculty of 'morphological assimilation', i.e. the building up and maintenance through metabolism of characteristic structure; on this depends 'morphological heredity', or the handing on of typical structure, together with the power of maintaining that structure. The lower orders of vital units depend upon 'chemical assimilation' for their continuance, and show only 'chemical heredity'. These grades of units have for us only a theoretical interest, and it is easy to see that Roux arrived at them merely by means of progressive abstraction; they are not necessarily 'real'. But Roux laid some stress on this line of thought, for it seemed to him to indicate how living beings, with all their apparently marvellous properties, could have evolved step by step from the isoplasson upwards, adding now one quality and now another, as these arose through variation and were perpetuated by selection. He sought in this way an escape from the conclusion that living beings show powers which are not

[1] See Roux, 1905, pp. 108–27.

explicable mechanically. We shall not follow out his argument, which is ingenious but unconvincing.

What is more important from our point of view is Roux's insistence on *metabolism* as the foundation of the other qualities of the organism. In morphological assimilation Roux saw 'the most general, most essential, and most characteristic formative activity of life'.[1] Through morphological assimilation form arises and form is maintained; assimilation is thus the basis of growth, development, and heredity.

'Assimilation in its different forms is the basis of this faculty of self-preservation and the preliminary condition of the self-formation of the individual, as of the continuity of the living thing, for the substance which produces this effect must in all its specific structure be renewed in metabolism and proliferate as well. *Accordingly only the variations which are capable of assimilation are heritable.* It can be said with wider significance that assimilation effects a kind of material memory, or the transference of the law of persistence from simple movements to those processes of form-production which are connected with metabolism' (1905, p. 108).

The principle here enunciated, that only those variations can be inherited which fall into, or share in, the metabolic cycle, is clearly a pregnant one.

Roux may perhaps best be described as a physiological morphologist. He was physiologist in that he insisted upon the importance of metabolism as the foundation of all form-production, all form-maintenance, and all form-change; he was morphologist in that he was interested primarily in form and not in physiological chemistry. His aim was to build up a new branch of biology, a science of the production of form, and this took him beyond the scope and methods of ordinary physiology, which is mainly concerned with the mode of action of the formed body, considered as a physico-chemical mechanism.

Although Roux clung firmly to the mechanistic theory as the only sound basis for exact science, he did attempt to take

[1] 'Ueber die Selbstregulation der Lebewesen', *Arch. Ent.-Mech.*, xiii, 1902 (pp. 610–50), p. 631.

up a position differing from that of the purely mechanistic physiologist. This position was not really intermediate, as he believed, between simple materialism and dualistic vitalism. He seems all the time to be striving after a position which should be distinctly biological and yet not in contradiction with the fundamental mechanistic standpoint which he adopts. But he is never quite successful in this attempt, and indeed the effect is foredoomed to failure, for the strict mechanistic point of view is incompatible with any real 'organismal' theory of living things.

As we have already seen (p. 98, above), Roux does not actually reach the conception of organism as something unitary and individual; he treats of vital properties in terms of metabolic processes; living *substance* regarded as a metabolic system is his ultimate concept, not the living organism, or even the living cell. The way was open to him when he seized the importance of 'complex components'—which are essentially the functions or activities of cells and organisms—but he did not take it. The conviction (arising from his mechanistic philosophy) that complex components must be analysed into simple components prevented him from seeing that a satisfactory middle position could be reached by linking up his complex components, which are functions, with the activity of the organism regarded as a unitary whole, and basing a distinctively biological method upon this conception of unity. He preferred to take the other course—that of progressive analysis, leading away from the conception of synthetic unity and 'wholeness'.

It must, however, be recognized that Roux was not far off recognizing the individuality of the living thing as something unique and different from anything in the inorganic sphere. We have already quoted a passage in which he speaks of the living being as something marked off by the 'Gesamtheit' of its functions from all inorganic bodies, and as possessing a certain 'Innerlichheit' (see p. 100, above). Another passage may be adduced in which he emphasizes the fact that living things are in no way artificial systems, but show a unique degree of autonomy and independence—

'Living things are not systems arbitrarily separated by us conceptually, but systems which demarcate themselves, and reproduce themselves through division and development, in which processes all, or almost all that is essential, is self-determined' (1905, p. 182). But it seems clear from a study of Roux's work as a whole that he considered organic systems to differ in degree and not in kind from inorganic systems, and both to be explicable in the long run on mechanistic principles.

We may turn now, after this discussion of Roux's general standpoint, to consider some of his more positive contributions to the understanding of development and heredity, of which we shall single out one or two of the most important. As I have tried to show in a previous work[1] Roux's greatest service to biology was his insistence on the importance of function and functional activity. He made a close study of functional adaptation and analysed the facts with much success. He was the first to realize and to demonstrate the great role that function plays in the development of form, and he established a valuable generalization regarding the relation of form to function at different stages of development. This was expressed first in his book *Die Kampf der Theile* (Leipzig, 1881), in which he wrote, 'There must be distinguished in the life of all the parts two periods, an embryonic in the broad sense, during which the parts develop, differentiate, and grow of themselves, and a period of completer development, during which growth, and in many cases also the balance of assimilation over dissimilation, can come about only under the influence of stimuli' (p. 180). There is thus a period of self-differentiation in which the organs are roughly formed in anticipation of functioning, and a period of functional development, in which the organs are perfected through functioning, and only through functioning. The two periods cannot be sharply separated from one another, nor does the transition from the one to the other occur at the same time in the different tissues and organs.

[1] *Form and Function*, 1916, pp. 316–29.

The conception is more fully expressed by Roux in 1905 as follows:

'This separation (of development into two periods) is intended only as a first beginning. The first period I called the embryonic period κατ' ἐξοχήν, or the period of organ rudiments. It includes the "directly inherited" structures, i.e. the structures which are directly predetermined in the structure of the germ-plasm, as, for instance, the first differentiation of the germ, segmentation, the formation of the germ-layers and the organ-rudiments, as well as the next stage of "further differentiation", and of *independent* growth and maintenance, that is, of growth and maintenance that take place without the functioning of the organs.

'This is accordingly the period of direct fashioning through the activity of the formative mechanism implicit in the germ-plasm, also the period of the self-conservation of the formed parts without active functioning.

'The second period is the period of "functional form-development". It includes the further differentiation and the maintenance in their typical form of the organs laid down in the first period; and this is brought about by the exercise of the specific functions of the organs. This period adds the finishing touches to the finer functional differentiation of the organs and so brings to pass the "finer functional harmony" of all organs with the whole. The formative activity displayed during this period depends upon the circumstance that the functional stimulus, or rather the exercise by the organs of their specific functions, is accompanied by a subsidiary formative activity, which acts partly by producing new form and partly by maintaining that which is already formed. . . . Between the two periods lies presumably a transition period, an intermediary stage of varying duration in the different organs, in which both classes of causes are concerned in the further building-up of the already formed, those of the first period in gradually decreasing measure, those of the second in an increasing degree' (1905, pp. 94–6).

Roux had in his earlier researches paid much attention to the process which is characteristic of second-stage development, namely, functional adaptation. He had shown, for instance, that the later development of the blood vessels comes about in direct response to functional requirements. Thus from the rudiments formed in the first period of development, before the system is properly functional, there

sprout out and grow the definitive blood-vessels supplying the tissues which have need of them. The size, direction, and intimate structure of these blood-vessels come to be accurately adjusted through functional adaptation to the part they play in the economy of the whole, and this adjustment or adaptation is brought about by the active response of the various tissues of which the blood-vessels are composed.[1]

The relation between the two stages of development naturally suggests the question—is it possible that characters which have been developed as second-stage characters in direct response to functional requirements can appear in later generations as first-stage characters, in advance of functioning? Roux was, at least in his early days, strongly inclined to the view that this transformation of second-stage characters into first-stage did take place in the course of many generations, and on this hypothesis he explained the transmissibility of acquired characteristics.

Speaking of the formative stimuli which are active in second-period development, Roux wrote in 1881: 'These stimuli can also produce new structure, which if it is constantly formed throughout many generations finally becomes hereditary, i.e. develops in the descendants in the absence of the stimuli, becomes in our sense embryonic' (1881, p. 180). Again, 'form-characteristics which were originally acquired in post-embryonic life through functional adaptation may be developed in the embryo without the functional stimulus, and may in later development become more or less completely differentiated, and retain this differentiation without functional activity or with a minimum of it. But in the continued absence of functional activity they become atrophied . . . and in the end disappear' (1881, p. 201).

The transmission of acquired characters certainly formed an element in Roux's earlier conceptions of heredity and development; he was of opinion that such transmission takes place in small degree and gradually, and that many generations are required before a new character can become

[1] See A. Oppel, *Ueber die gestaltliche Anpassung der Blutgefässe* (containing a long section by W. Roux), Roux's *Vorträge und Aufsätze*, x, Leipzig, 1910.

hereditary. It should be noted however that these views date from before the establishment of the germ-plasm doctrine.

Roux paid much attention not only to normal development, particularly in its functional aspect, but also to the response of the developing organism to abnormal conditions, whether external or internal—to the problem of autonomy and regulation. It was one of the great services of experimental embryology that it showed how widespread and important such regulatory processes are—and how difficult to explain.

Roux distinguished two main kinds of development—typical and regulatory. Typical development is found when the hereditary equipment of the germ and the conditions of development are both 'normal'. It is the production of typical form in the typical way. Regulatory development on the other hand builds up, in spite of atypical germinal beginnings or abnormal environmental conditions, the typical form of the organism (1905, p. 76). It is shown very clearly in all cases of restitution and regeneration. Typical development as a matter of fact never actually takes place, for the least departure from the typical course of development calls forth into activity the mechanisms of self-regulation. Much of normal development is in reality regulatory, for instance, most processes of functional adaptation.

Regulatory development is much more difficult to explain mechanistically than typical development. In typical development there is much that is automatic and mechanical, and therefore susceptible of strict analysis. In the 'first period' at least, typical development takes a more or less habitual and unchanging course, and each part shows a considerable degree of independence and a certain power of self-differentiation. Regulatory development on the other hand shows a disconcerting spontaneity, and is governed in a mysterious manner by the condition of the organism as a whole or at least of large parts of it (1905, p. 72). Regulatory development is much more a living, responsive activity of the organism than is typical development, and it is to this degree

less easy to explain. It was the extraordinary purposiveness of regulatory phenomena that led many investigators, e.g. G. Wolff and H. Driesch, to assume the intervention in development of a vitalistic agent.

Roux, as we have seen, did not accept this vitalistic conclusion. He held that the riddle is not quite so insoluble as it seems at first sight. He pointed out that no new tissue-qualities are implied in regulatory processes, beyond those that may be conceived to have arisen through natural selection, in the course of the evolution of the primal organisms from isoplassons and idioplassons. Many cases of regeneration could, he thought, be explained on the hypothesis that reserve idioplasm is stored in the chromosomes of the somatic cells ready to regenerate lost parts.

Even from the slight sketch of Roux's work which we have given it will be apparent that there were few of the great problems of development and heredity which he did not touch upon and illuminate. We have seen with what skill and assiduity he treated the problems of differentiation, bringing to light the very important distinction between first-stage and second-stage development, and emphasizing the role that function plays in the moulding of form. We have seen that although he accepted in its main lines the germ-plasm theory as an adequate explanation of heredity, he tried to interpret it physiologically rather than morphologically, recognizing that the germinal substance must show the fundamental characteristics of morphological assimilation and self-regulation, and not be merely a static configuration passively handed down. Its self-identity or continuity was not something fixed and rigid, but a state constantly destroyed and constantly restored through metabolism and regulation. His physiological point of view puts him in advance of Weismann, whose treatment of the problems of development and heredity was, as we have seen, schematic and formal. In his early theory of the phylogenetic relation between the two stages of development he opened the way to a rational explanation of the fact of recapitulation. Methodologically, he came near to a functional or organismal treatment of

living things, but was held back from full acceptance of this point of view by his deep-rooted belief in mechanism.

The last twenty years of the nineteenth century saw an immense amount of work carried out on the problems of experimental embryology, a great accession of new facts, and a lively interest in the philosophical questions which they inevitably raised. Typical of the new experimental school was its insistence on the importance of environment; its main interest was the study of the developing organism regarded as actively responding to its surroundings,[1] and not as a static mechanism such as morphology had conceived it.

It is not my intention to treat this period historically; all we need note here is that the majority of workers held fast to mechanistic views and attempted to apply physiological methods of explanation; some of these views we have discussed in the last chapter. There was, however, an important minority who felt that a mechanistic explanation of the new facts was in principle impossible, and fell back accordingly upon a dualistic vitalism. Noteworthy among these were G. Wolff[2] and H. Driesch. I have elsewhere[3] given my reasons for rejecting the vitalism of Driesch, and do not propose to discuss his theories[4] in detail in this book; they do not seem to lead *in practice* to a method of attack upon the problems in any way different from the mechanistic, and they have already been fully treated both by Driesch and by his critics. The controversy between mechanism and vitalism, having raged fiercely for years, has now died down. Let us not revive it!

[1] See particularly C. Herbst, *Formative Reize in der tierischen Ontogenese*, Leipzig, 1901.

[2] *Arch. f. Ent.-Mech.* i, pp. 380–90, 1895; *Beiträge zur Kritik der Darwinschen Lehre*, Leipzig, 1898.

[3] *The Study of Living Things*, 1924, pp. 20–6.

[4] *The Science and Philosophy of the Organism* (Gifford Lectures), 2 vols., London, 1908. New edition in one vol., 1929. In German as *Philosophie des Organischen*, Leipzig, 1909, 2nd edit., 1921. *Ordnungslehre*, Jena, 1912, 2nd edit., 1923. Driesch's earlier 'analytic theory of organic development' (1894) is dealt with adequately by J. W. Jenkinson, *Experimental Embryology*, Oxford, 1909, pp. 280–6.

VIII

THE MNEMIC THEORIES

ALTHOUGH Samuel Butler was not the first to enunciate a theory linking up development with memory—this honour belongs to Hering—it is convenient to begin with him, for his point of view is radically different from that adopted in most theories of development, and represents in fact an entirely new method of approach. As we shall see later, the theories of Hering and Semon remain based upon a materialistic conception of the organism and show little methodological advance upon the views current in their time. Butler, on the other hand, whether he was right or wrong, did strike out for himself a new line, and by adopting a frankly psychological standpoint was able to look at heredity and development from a new angle.

Butler was not a professional biologist, and therein lay both his strength and his weakness. He was the cultivated amateur, bringing to bear upon a great problem, whose intricacies he perhaps did not fully realize, a keen, ingenious, and unbiassed mind. We must remember too that when he published his main book on biological problems, *Life and Habit* (1878), the detailed facts about the nature of fertilization had not long been discovered, and had barely had time to filter down from the technical journals to the man in the street; the germ-plasm theory had not yet been formulated by Weismann; it was still orthodox to believe in the inheritance of acquired characters, and Charles Darwin had even revived the ancient Hippocratic doctrine of pangenesis in order to explain such transmission on a materialistic basis.

In order to understand Butler's point of view it is necessary to free one's mind from such modern conceptions as the germ-plasm theory, the separation of soma and germ-cells, and to hark back to a simpler, almost 'pre-scientific' view. It is in fact the very simplicity of Butler's theory that makes it rather difficult to grasp at the present day. The cell-theory

was familiar to him, and he knew that fertilization consisted in the union of two cells, the ovum and the spermatozoon, but there his knowledge stopped. He thought habitually in terms of the organism as a whole and did not, as we do, think of it in terms of cells. Thus for him the hen did really form the egg, just as a plant may form a bud or a tuber; he did not trouble himself about the cellular details. We shall find it impossible to understand what Butler is driving at unless we can by an effort recover his pre-Weismannian simplicity of outlook.

Butler hit upon the memory-theory of heredity in complete independence of Hering, who preceded him actually by eight years. Only after his book was published did he hear of Hering, and he rendered graceful homage to his predecessor by giving an excellent translation of Hering's lecture in his *Unconscious Memory* (1880). Some hint or foreshadowing of Butler's views is found in Erasmus Darwin's *Zoonomia* (i, 1794), as he himself points out, quoting the following passage: 'Owing to the imperfection of language, the offspring is termed a new animal; but is, in truth, a branch or elongation of the parent, since a part of the embryonic animal is or was a part of the parent, and, therefore, in strict language, cannot be said to be entirely new at the time of its production, and, therefore, it may retain some of the habits of the parent system' (p. 484).

Butler introduces his theme in *Life and Habit* by pointing out and illustrating how great a part habit plays in the individual life; we all know that complex actions and trains of action at first laboriously and consciously learnt become easy and habitual through long-continued practice, reaching finally the unconsciousness and automaticity of perfect habit, or as Butler would say, of perfect knowledge. The analogy of development and habitual action is striking. All goes on *as if* the embryo had perfect knowledge of the route to follow, and this in Butler's view can only be because it has already gone through its development countless times before, so that its knowledge has become automatic and unconscious.

Is it conceivable, asks Butler, that the embryo can do all

the things that it does without knowing how to do them, and without having done them before?

'Shall we say', he writes, 'that a baby of a day old sucks (which involves the whole principle of the pump, and hence a profound practical knowledge of the laws of pneumatics and hydrostatics), digests, oxygenizes its blood (millions of years before Sir Humphrey Davy discovered oxygen), sees and hears—all most difficult and complicated operations, involving a knowledge of the facts concerning optics and acoustics, compared with which the discoveries of Newton sink into utter insignificance? Shall we say that a baby can do all these things at once, doing them so well and so regularly, without being even able to direct its attention to them, and at the same time not know how to do them, and never have done them before?[1]

Assuredly not.

There must therefore be a real continuity of experience between the embryo and its parents, and, through the endless chain of ancestors, right back to the dawn of life. The kernel of Butler's theory is this extension of habit and memory beyond the confines of the individual life. To explain development as being due to habit:

'. . . we must suppose the continuity of life and sameness between living beings, whether animals or plants, and their descendants, to be far closer than we have hitherto believed; so that the experience of one person is not enjoyed by his successor, so much as that the successor is *bona fide* but a part of the life of his progenitor, imbued with all his memories, profiting by all his experiences—which are, in fact, his own—and only unconscious of the extent of his own memories and experiences owing to their vastness and already infinite repetitions' (ibid., p. 50).

It will be readily admitted that there is continuity in the life of the individual from ovum to old age:

'Nor, if we admit personal identity between the ovum and the octogenarian, is there any sufficient reason why we should not admit it between the impregnate ovum and the two factors of which it is composed, which two factors are but offshoots from two distinct personalities, of which they are as much part as the apple is of the apple-tree; so that an impregnate ovum cannot without a violation of first principles be debarred from claiming personal identity with both

[1] *Life and Habit.* Fifield reprint, 1910, p. 54.

its parents, and hence, by an easy chain of reasoning, *with each of the impregnate ova from which its parents were developed*.

'So that each ovum when impregnate should be considered not as descended from its ancestors, but as being a continuation of the personality of every ovum in the chain of its ancestry, which every ovum *it actually is* quite as truly as the octogenarian *is* the same identity with the ovum from which he has been developed.

'This process cannot stop short of the primordial cell, which again will probably turn out to be but a brief resting-place. We therefore prove each one of us to *be actually* the primordial cell which never died nor dies, but has differentiated itself into the life of the world, all living beings whatever being one with it, and members one of another' (ibid., pp. 85–6).

It is a little unfortunate that Butler uses the words 'personal identity' to describe what is neither more nor less than continuity of organic experience—the emphasis should be laid on 'continuity' rather than upon 'personality'. But the meaning of the words is perfectly clear, and is nowhere more vividly brought out than in the following passage from *Luck and Cunning* (1887) where the race is declared to be 'one long individual, living indeed in pulsations, so to speak, but no more losing continued personality by living in successive generations than an individual loses it by living in consecutive days' (Fifield reprint, 1909, p. 25). Instead of continuity of germ-plasm we have here continuity of living experience.

It is important to note that the egg or embryo is regarded as actually partaking in the life of its producer, as actually sharing the hereditary experience of the parent organism. Butler does not seem to have realized the fact that the germ-cells live as it were a life of their own and go through a special development, separate from the differentiation of the soma, and having reference chiefly to their future destiny as eggs or sperms. If he did recognize the fact, he seems to have thought it of subordinate importance. His conception is that the gametes actually share in the experience of the parents, just as a bulb, or tuber, or cutting of a plant may be assumed to 'know whatever the plant knows'. There is no question of an influence exerted by the soma upon the germ-cells (such as is required in the theories of Hering and Semon),

for Butler did not separate the two. This is the point where, in the light of modern conceptions, Butler's theory is difficult to follow. One must however make the required effort to grasp his thought. It emerges fairly clearly from the following, apparently cryptic, sentence: 'A moth becomes each egg that she lays, and that she does so, she will in good time show by doing, now that she has got a fresh start, as near as may be what she did when first she was an egg, and then a moth, before' (*Life and Habit*, p. 99).

The egg or embryo (and also the spermatozoon) is to be regarded as a bud of the parent, summarizing all the experience of that parent—all its developmental tendencies and all its instincts—up to the time when it leaves the body of the parent. As the parent itself was produced from egg and sperm, the chain of experience is continuous back to the previous generation, and so, generation by generation, right back to the primordial form from which life has sprung. It is in this simple sense that we are to interpret Butler's conclusion in the last pages of *Life and Habit* that 'the small, structureless, impregnate ovum from which we have each one of us sprung, has a potential recollection of all that has happened to each one of its ancestors prior to the period at which any such ancestor has issued from the bodies of its progenitors—provided that is to say, a sufficiently deep, or sufficiently often-repeated, impression has been made to admit of its being remembered at all' (p. 297).

What light does the theory of ancestral habit throw upon the problems of development? In the first place, it accounts for the orderly succession of stages in ontogeny, for the embryo goes through these as by routine, each stage awakening the memory of what to do next. On the memory theory:

'Each step of normal development will lead the impregnate ovum up to, and remind it of, its next ordinary course of action, in the same way as we, when we recite a well-known passage, are led up to each successive sentence by the sentence which has immediately preceded it. . . . Hence, though the ovum immediately after impregnation is instinct with all the memories of both parents, not one of these memories can normally become active till both the ovum itself, and

its surroundings, are sufficiently alike what they respectively were, when the occurrence now to be remembered last took place. The memory will then immediately return, and the creature will do as it did on the last occasion that it was in like case as now. This ensures that similarity of order shall be preserved in all the stages of development, in successive generations' (pp. 297–8).

It accounts also for heredity, and in particular for the fact that the offspring as a rule resembles its own parents more than any chance pair of the stock, for on the memory theory we should expect 'that the offspring should, as a general rule, resemble its own most immediate progenitors; that is to say, that it should remember best what it has been doing most recently' (p. 168).

In particular—and this is one of the strongest points of the mnemic theory—it explains why in the first period of development structure is formed in advance of functioning, and why in a general way the embryo repeats in ontogeny the ancestral history of its race. As Butler writes:

'The self-development of each new life in succeeding generations—the various stages through which it passes (as it would appear, at first sight, without rhyme or reason)—the manner in which it prepares structures of the most surpassing intricacy and delicacy, for which it has no use at the time when it prepares them—and the many elaborate instincts which it exhibits immediately on, and indeed before, birth—all point in the direction of habit and memory, as the only causes which could produce them.

'Why should the embryo of any animal go through so many stages—embryological allusions to forefathers of a widely different type? And why, again, should the germs of the same kind of creature always go through the same stages? . . .

'The creature goes through so many intermediate stages between its earliest state as life at all, and its latest development, for the simplest of all reasons, namely, because this is the road by which it has always hitherto travelled to its present differentiation; this is the road it knows, and into every turn and up and down of which, it has been guided by the force of circumstances and the balance of considerations' (pp. 125–6).

It accounts for the fact that the development of the individual is only a shortened and sketchy epitome of the

developmental history of its ancestors, not recapitulating this in full, but taking short cuts and telescoping stages. 'In its earliest stages the embryo should be simply conscious of a general method of procedure on the part of its forefathers, and should, by reason of long practice, compress tedious and complicated histories into a very narrow compass, remembering no single performance in particular' (p. 169).

Butler was of course an ardent Lamarckian[1] and believed firmly that advance in evolution takes place only by the effort of the organism itself. Such effort, he conceived, as did Roux about the same time (see above, p. 108), made its mark upon succeeding generations, so that what was originally acquired by pain and striving made its appearance more easily in succeeding generations and finally without any effort at all—in the absence of the functional stimulus, as Roux would say.

In general, Butler conceived normal development to be a blind and automatic repetition of ancestral routine, out of which sleep-like progression the embryo is stirred only when it encounters unusual or difficult circumstances, such as it has in the person of its ancestors rarely or never met with before. When it is thus stirred out of its routine it has to cope actively with the unusual situation, with the results that we see in regulatory development.

'When events are happening to it which have ordinarily happened to its forefathers, and which it would therefore remember, if it was possessed of the kind of memory which we are here attributing to it, *it acts precisely as it would act if it were possessed of such memory.*

'When, on the other hand, events are happening to it, which, if it has the kind of memory we are attributing to it, would baffle that memory, or which have rarely or never been included in the category of its recollections, *it acts precisely as a creature acts when its recollection is disturbed, or when it is required to do something which it has never done before*' (*Life and Habit*, p. 132).

The mnemic theory is of course peculiarly adapted to explain the historical or routine aspect of development; it does not by itself explain the driving force or hormic impulse behind development, nor the initiative shown by the embryo

[1] See *Evolution Old and New*, London, 1879.

in adapting itself to unusual conditions. At the most it gives a reasoned account of why the developmental impulse follows such and such routine paths, is so curiously indirect, and yet is so orderly a succession of events. Butler's own theory of evolution by effort supplies, to some extent at least, this missing element in the mnemic conception.

Butler made his memory theory rather more difficult than it needed to be by bringing in consciousness as a necessary accompaniment of the organism's original effort—of that effort which, through practice, throughout a long series of generations, becomes in time habitual and unconscious.

He really had no warrant in experience for assuming that 'organic' or growth-activities, as distinct from behaviour-activities, are ever consciously performed, for the only actions which we consciously will are behaviour-actions carried out vis-à-vis a sensed environment. Nor is evidence lacking that the phenomena of habit and learning can be manifested by tissues and organs, as is seen in many cases of functional adaptation, where there is not the slightest justification for assuming *conscious* guidance.

We turn now to a consideration of Butler's philosophic standpoint. Here again we find the amateur, full of brilliant ideas, but unable to weave them into a fully coherent system. He was definitely anti-materialist, and combated the materialistic side of Charles Darwin's doctrine of evolution, preferring to it the older teleological views of Erasmus Darwin and Lamarck. He took the ordinary, everyday, 'commonsense' view of living things, seeing them as active, striving individuals, beating out a livelihood by means of their own efforts. Survival he considered was not a matter of luck, as Charles Darwin's theory seemed to imply, but a matter of the organism's own ingenuity—and this gave the title to his last book on biological problems, *Luck or Cunning* (1887).

We do not find in Butler's writings any formal statement of his philosophical position. It may best be described as psychobiological. He was convinced that it was hopeless to explain life in terms of matter only, and that instead of

regarding living things as on a level with inorganic objects, differing only by degree of material complexity, it was necessary rather to assimilate the inorganic to the organic.

'The only thing of which I am sure', he wrote in *Unconscious Memory* (1880), 'is, that the distinction between the organic and inorganic is arbitrary; that it is more coherent with our other ideas, and therefore more acceptable, to start with every molecule as a living thing, and then deduce death as the breaking up of an association or corporation, than to start with inanimate molecules and smuggle life into them; and that, therefore, what we call the inorganic must be regarded as up to a point living, and instinct, within certain limits, with consciousness, volition, and power of concerted action' (Fifield reprint, 1910, p. 15).

Later, in 1887, he definitely accepts a sort of pampsychism, refusing to think of soul in isolation from body, or of body in isolation from soul.

'All body', he writes, in *Luck and Cunning*, 'is more or less ensouled. As it gets farther and farther from ourselves, indeed, we sympathize less with it; nothing, we say to ourselves, can have intelligence unless we understand all about it—as though intelligence in all except ourselves meant the power of being understood rather than that of understanding. We are intelligent, and no intelligence, so different from our own as to baffle our powers of comprehension, deserves to be called intelligence at all. The more a thing resembles ourselves, the more it thinks as we do—and thus by implication tells us that we are right—the more intelligent we think it; and the less it thinks as we do, the greater fool it must be; if a substance does not succeed in making it clear that it understands our business, we conclude that it cannot have any business of its own, much less understand it, or indeed understand anything at all.

'But letting this pass, so far as we are concerned, *χρημάτων πάντων μέτρον ἀνθρωπος*, we are body ensouled, and soul embodied, ourselves, nor is it possible for us to think seriously of anything so unlike ourselves as to consist either of soul without body, or body without soul' (Fifield reprint, 1909, p. 80).

There is noticeable in these two quotations a certain measure of approach to the 'organic theory' of Nature later elaborated from a different standpoint by Whitehead (see below, p. 179 et seq.), and it is hardly fanciful to see in the

following two (also from *Luck and Cunning*) a distinctly Bergsonian turn of thought.

'Action may be regarded as a kind of middle term between mind and matter; it is the throe of thought and thing, the quivering clash and union of body and soul; commonplace enough in practice; miraculous, as violating every canon on which thought and reason are founded, and we theorize about it, put it under the microscope, and vivisect it' (p. 79).

'All change is *qua* us absolutely incomprehensible and miraculous; the smallest change baffles the greatest intellect if its essence, as apart from its phenomena, be inquired into' (p. 76).

Before leaving Samuel Butler, it is interesting to note that he did consider—and reject—the materialistic alternative to his memory theory. It was pointed out to him by a critical friend that the accurate repetition of the developmental cycle might be simply explained by assuming, as in the germ-plasm theory, identity of starting-point. If the antecedents were identical we should expect identical consequences. Butler discusses this possibility at some length in *Unconscious Memory*.

'I endeavoured to see', he writes, 'how far I could get on without volition and memory, and reasoned as follows: A repetition of like antecedents will be certainly followed by a repetition of like consequents, whether the agents be men and women or chemical substances' (p. 153).

There are all sorts of inorganic cycles, in which memory clearly plays no part:

'Who will attribute memory to the hands of a clock, to a piston-rod, to air or water in a storm or in course of evaporation, to the earth and planets in their circuits round the sun, or to the atoms of the universe, if they too be moving in a cycle vaster than we can take account of. And if not, why introduce it into the embryonic development of living beings, when there is not a particle of evidence in support of its actual presence, when regularity of action can be ensured just as well without it as with it, and when at the best it is considered as existing under circumstances which it baffles us to conceive, inasmuch as it is supposed to be exercised without any conscious recollection. Surely a memory which is exercised without any consciousness of recollecting is only a periphrasis for the absence of any memory at all' (p. 160).

The answer is that we *must* bring memory in to account for development, for it is one of the antecedents. If we deny this psychical element in development we must by analogy deny it also in human behaviour.

If the repetition of the course of development were exact we might perhaps believe it to be mechanical.

'The fact . . . that on each repetition of the action there is one memory more than on the last but one, and that this memory is slightly different from its predecessor, is seen to be an inherent and, *ex hypothesi*, necessarily disturbing factor in all habitual action—and the life of an organism should be regarded as the habitual action of a single individual, namely, of the organism itself, and of its ancestors' (p. 167).

'If we observed the resemblance between successive generations to be as close as that between distilled water and distilled water through all time, and if we observed that perfect unchangeableness in the action of living beings which we see in what we call chemical and mechanical combinations, we might indeed suspect that memory had as little place among the causes of their action as it can have in anything, and that each repetition, whether of a habit or the practice of an art, or of an embryonic process in successive generations, was an original performance, for all that memory had to do with it. I submit however that in the case of the reproductive forms of life we see just so much variety in spite of uniformity, as is consistent with a repetition involving not only a perfect similarity in the agents and their circumstances, but also the little departure therefrom that is inevitably involved in the supposition that a memory of like presents as well as of like antecedents (as distinguished from a memory of like antecedents only) has played a part in their development—a cyclonic memory, if the expression may be pardoned' (p. 173).

One is reminded of a subtle and profound remark in *Evolution, Old and New*: 'It is not in the bond or *nexus* of our ideas that something utterly inanimate and inorganic should scheme, design, contrive, and elaborate structures which can make mistakes; it may elaborate low unerring things, like crystals, but it cannot elaborate those which have the power to err' (Jonathan Cape reprint, p. 29).

Samuel Butler's psychological or psychobiological point of view found few adherents in scientific circles, though Hartog

and Darbishire in this country showed much sympathy with and understanding of his views.[1] Strongest support came from that fine philosopher James Ward, who discussed the memory theory in his *Realm of Ends* (2nd edit., 1912) and also in a valuable little essay *Heredity and Memory* (Cambridge, 1913), in which he pointed out that the memory theory could be properly used only by those who adopt, as did Butler, a frankly psychological attitude. Referring to Semon's theory, he wrote:

'Records or memoranda alone are not memory, for they presuppose it. *They* may consist of physical traces, but memory, even when called "unconscious", suggests mind; for, as we have seen, the automatic character implied by this term "unconscious" presupposes foregone experience.... The mnemic theory then, if it is to be worth anything, seems to me clearly to require not merely physical records or "engrams", but living experience or tradition. The mnemic theory will work for those who can accept a monadistic or pampsychist interpretation of the beings that make up the world, who believe with Spinoza and Leibniz that "all individual things are animated albeit in divers degree". But quite apart from difficulties of detail, I do not see how in principle it will work otherwise' (pp. 55–6).

Hering's views, which we have hitherto passed over, are contained in a lecture, delivered in 1870, entitled 'Ueber das Gedächtniss als eine allgemeine Funktion der organisirten Materie' (Vienna).[2]

Ewald Hering was a highly skilled physiologist who did excellent work on visual sensations, and his exposition, though short, is better documented than Butler's and carries more conviction to the professional mind. It is written from the point of view of the physiologist.

His philosophical position is that of psycho-physical parallelism. The physiologist, he maintains, must treat the organism as purely material, though the psychologist has an

[1] Marcus Hartog, *Problems of Life and Reproduction*, London, 1913; A. D. Darbishire, *An Introduction to a Biology*, London, 1917. See also C. J. Patten, *The Memory Factor in Biology*, London, 1926. F. Darwin's views are considered below (pp. 129–30).

[2] Reprinted in Ostwald's 'Klassiker der exakten Wissenschaften', No. 148, 1921. Translated in Butler's *Unconscious Memory* (1880, pp. 97–133), also with two other lectures in *Memory*, Open Court Pub. Co., 4th edit., 1913, Chicago and London.

equal right to regard only the psychical side. Material and psychical events in the living thing are functions one of the other. The physiologist may even on occasion shift his attention to the psychical side, provided he does this advisedly and does not confuse psychical with physical concepts. What the material aspect of life does not reveal to his inquiry he may find displayed in the mirror of consciousness.

It is in regarding this mirror, in consulting the data of his own experience, that he becomes aware of the importance of memory and habit. But he finds too that memory is not always conscious—the chain of recollections is continuous, but only at times conscious. 'Between the "me" of to-day and the "me" of yesterday lie night and sleep, abysses of unconsciousness; nor is there any bridge but memory with which to span them' (Butler's transl.). Yet memory does span them and the bond of union lies in our unconscious world.

'Thus the cause which produces the unity of the single phenomena of consciousness must be looked for in unconscious life. As we know nothing of this except what we learn from our investigations of matter, and since in a purely empirical consideration matter and the unconscious must be regarded as identical, the physiologist may justly define memory in a wider sense to be a faculty of the brain, the results of which to a great extent belong to both consciousness and unconsciousness' (Open Court trans., p. 9).

The physiologist must, if he wishes to use this concept of memory in a scientific and objective manner, return to the mechanistic point of view and regard memory as a property of organized matter; he must disregard its psychical aspect. From this point of view, memory depends upon a material trace or impression made upon living matter by the original situation which is later 'remembered'. The evidence from experience 'clearly shows that after the extinction of conscious sensations, some material vestiges still remain in our nervous system, implying a change of its molecular and atomic structure, by which the nervous substance is enabled to reproduce such physical processes as are connected with the corresponding physical processes of sensation and perception'

(p. 7). Such recollected perceptions may arise in the absence of the external stimulus which originally called them forth.

Habit and memory play a part not only in behaviour-life, but also in other organic activities. A muscle grows stronger by use and increases in size; this law of functional adaptation holds good for most organs and tissues, and is clearly a manifestation of organic memory. In cell division and multiplication we see another manifestation of the same power of organic memory or reproduction, and the most striking of all in the development of the individual organism. Hering considered, as did most biologists of his time, that there was ample evidence of the transmissibility of acquired characters. Every organism, he thought, adds a small heritage of personal acquisition to the hereditary equipment of its gametes. How this comes about is difficult to understand; it may be through the instrumentality of the all-pervading nervous system or by way of the body fluids, but it is certain that the destinies of the growing organism are in some way re-echoed in the germ-cells. We have to do here not with any immaterial influence; the specific material structure of the germ determines its future development, and the parental organism can affect this development only by influencing materially, it may be in an infinitesimal degree, the specific germinal architecture.

'If', then, 'in a parental organism by long habit or constant practice something grows to be second nature, so as to permeate, be it ever so feebly, its germinal cells, and if the germinal cells commence an independent life, they increase and grow till they form a new being, but their single parts still remain the substance of the parental being, they are bones of its bones, and flesh of its flesh. If, then, the filial organisms reproduce what they experienced as a smaller part of a greater whole, this fact is marvellous indeed, but no more so than when an old man is surprised by reminiscences of his earliest childhood' (pp. 16–17).

If the parents' acquired characters can thus be reproduced by each offspring, how much more will it reproduce those characters which have for countless generations been developed by its ancestors, and so have been deeply impressed

upon the organic memory of the germ-cells. 'Thus every organized being of our present time is the product of the unconscious memory of organized matter. Constantly increasing and dividing, constantly assimilating new and excreting waste matter, constantly recording new experiences in its memories, to be reproduced again and again, each has taken richer and more perfect shape the longer it has lived' (p. 18).

It is a natural consequence of this ancestral memory that the developing organism should run through in a summary way the principal stages of the evolution of its race.

It will be seen that Hering's views on heredity and memory are in practice not very different from those later propounded by Butler. They were, however, definitely grounded in a mechanistic conception of life—hence the insistence that memory depends on material traces, and is to be considered as a function of organized *matter*; hence too the supposition that the soma must in some way exercise a material influence upon the germ-cells. We shall see presently how Richard Semon some thirty years later developed these mechanistic assumptions of Hering's theory.

In passing, it is worth noting, in justice to Hering, that in a later essay (1898) he protested against a too facile application of mechanistic conceptions to physiology, and pointed out that 'Life can be *fully* understood only from life, and a physics and a chemistry which have sprung up solely from the domain of inanimate nature are adequate only to the explanation of such things as are common to the living and the dead.'[1]

Hering stated his mnemic theory merely in outline; it was left to the zoologist Richard Semon to develop and elaborate Hering's conception.[2] It is not necessary to examine Semon's views in detail; his treatment of the theme is analytic and of a Germanic thoroughness, but the fundamental ideas are the

[1] Open Court publication, 1913, p. 45.

[2] R. Semon, *Die Mneme*, Leipzig, 1904. English translation by L. Simon from third German edition (1911), London, 1921. The mnemic idea was developed to some extent by Haeckel (1876), also by E. D. Cope (1885, 1889, and 1896), and particularly by H. B. Orr (1893).

same as Hering's. He sets out to prove that all 'reproductive' processes, whether of heredity, habit, or memory, are due to one and the same property of organized matter—the *mneme*. Repetition of a train of events is of course not confined to the organic world, but it is a peculiarity of mnemic reproduction that it is independent of a complete repetition of the original conditions. Often a very small portion of the original situation suffices to cause a reproduction of the original reaction.

The mnemic property is regarded purely from the physiological point of view. Any stimulus acting upon irritable organic substance not only produces an immediate physical effect but leaves behind it an enduring physical trace or *engram*. Subsequent stimuli of a similar *or associated* kind elicit an *ecphoric* response. The main object of Semon's book is 'to deduce from a common property of all irritable organic substance—namely, that of retaining revivable traces or engrams—a number of mnemic laws, equally valid for the reproductions commonly grouped under memory, habit, or training, and also for those which come under the head of ontogenetic development, inherited periodicity, and regeneration—laws common, in fact, to every kind of organic reproduction' (p. 13).

The principle mnemic laws are as follows:

'*The First Mnemic Law*, or *Law of Engraphy*. All simultaneous excitations within an organism form a coherent simultaneous excitation-complex which acts engraphically; that is, it leaves behind a connected engram-complex constituting a coherent unity.

'*The Second Mnemic Law, or Law of Ecphory*. The partial recurrence of the energetic condition, which has previously acted engraphically, acts ecphorically on the whole simultaneous engram-complex; or, as it may be more explicitly stated: the partial recurrence of the excitation-complex, which left behind the engram-complex, acts ecphorically on this simultaneous engram-complex, whether the recurrence be in the form of an original or of a mnemic excitation.

'Association is the nexus of the single components of an engram-complex. The engram-association is a result of engraphy and becomes manifest in ecphory' (pp. 273–4).

The more purely psychological side of Semon's inquiry

into mnemic phenomena was further pursued (from a parallelistic standpoint) in two subsequent publications,[1] but we are here concerned only with the application of the mnemic principle to the problems of development and heredity. Semon was firmly convinced that the engraphic effects of stimuli in the individual could be, at least in certain cases, transmitted to its descendants, and he discussed in a very useful volume[2] the general evidence for the transmission of acquired characters. Exactly how this engraphic effect reaches the germ-cells is not made clear, but Semon holds that 'somatic induction' is more probable than 'parallel induction'—in other words, that the effect on the germ-cells is mediated through the somatic modification rather than imposed simultaneously on soma and germ-cells. The germ-cells appear to pass through a period of special sensitiveness to impressions from the soma.

The germ-cells contain the complete inherited engram-stock of the species, and development is due to the ecphory of these material predispositions. Semon does not enter into much detail concerning this 'engrammatic' conception of the germ-plasm, nor does he definitely locate the engram-stock in any particular constituent of the germ-cell. His general position is that 'each germ-cell, or its equivalent, which initiated each individuality phase, possesses the entire inherited engram-stock. Most probably neither the cell nor the nucleus of the cell is the smallest unit able to possess it. For the sake of brevity, we shall call the smallest unit able to contain the entire inherited engram-stock the "mnemic protomer"; whether it be the cell, or whether it be a more minute morphological unit, we shall leave future research to decide' (p. 116). The facts of regeneration show that such mnemic protomers must exist widely distributed throughout the developing organism.

There is an obvious resemblance between Semon's protomers and Weismann's ids, but Semon was fully aware of the

[1] *Die mnemischen Empfindungen*, Leipzig, 1909, 2nd edit., 1922; *Bewusstseinsvorgang und Gehirnprozess*, Wiesbaden, 1920.
[2] *Das Problem der Vererbung 'erworbener Eigenschaften'*, Leipzig, 1912.

danger of postulating morphologically distinct representative particles. 'Useful as such symbolic ideas may be for purposes of Mendelian research', he writes, 'the materialization of symbols in the shape of morphologically isolable units appears to me a very dangerous procedure' (p. 252). Semon adopted the same general philosophical position as Hering—that for the purposes of science attention must be focussed on the material side of organic happenings. Like Semon he stated the essentially psychological concept of the mneme in terms of material traces or engrams.

An interesting variant of the mnemic theory is that propounded by the late Prof. Rignano,[1] where the idea is applied to the organism regarded as a developing physico-chemical *system*.

Perhaps the most persuasive advocate of the mnemic theory—certainly in this country—was the late Sir Francis Darwin, who dealt with it in his illuminating Presidential Address to the British Association in 1908.[2]

He follows Semon on the whole and accepts the engram idea, widening it however to cover the 'internal conditions' of Pfeffer and of Klebs, and the 'physiological states' of Jennings, from the works of whom, and from his own experiments with plants, he draws a wealth of illustration of mnemic phenomena. He makes the important point that just as the study of movements requires their analysis in terms of stimulus and response, so the same procedure must be adopted in the study of morphological changes. This has the important result 'that the dim beginnings of habit or unconscious memory that we find in the movements of plants and animals must find a place in morphology', and particularly in the study of development.

His main conclusions regarding the deep-rooted analogy between habit and development may be summarized as follows:

'The development of the individual from the germ-cell takes place

[1] E. Rignano, *Sur la transmissibilité des caractères acquis*, Paris, 1906, Eng. Trans. by B. C. H. Harvey, Chicago, 1911.

[2] British Association Report for 1908, pp. 1–27.

by a series of stages of cell-division and growth, each stage apparently serving as a stimulus to the next, each unit following its predecessor like the movements linked together in an habitual action performed by an animal. My view is that the rhythm of ontogeny is actually and literally a habit. It undoubtedly has the feature which I have described as pre-eminently characteristic of habit, viz., an automatic quality which is seen in the performance of a series of actions in the absence of the complete series of stimuli to which they (the stages of ontogeny) were originally due. This is the chief point on which I wish to insist—I mean that the resemblance between ontogeny and habit is not merely superficial, but deeply seated' (p. 14).

We may quote also his reference to the theory of recapitulation and its explanation in terms of the mnemic conception.

'Again, there is the wonderful fact that, as the ovum develops into the perfect organism, it passes through a series of changes which are believed to represent the successive forms through which its ancestors passed in the process of evolution. This is precisely paralleled by our own experience of memory, for it often happens that we cannot reproduce the last-learned verse of a poem without repeating the earlier part; each verse is suggested by the previous one and acts as a stimulus for the next. The blurred and imperfect character of the ontogenetic version of the phylogenetic series may at least remind us of the tendency to abbreviate by omission what we have learned by heart' (p. 15).

He believes of course in the transmissibility of acquired characters and the mnemic connexion of each generation with the next. 'This can only be possible if the germ-cells are, as it were, in telegraphic communication with the whole body of the organism, so that as ontogeny is changed by the addition of new characters, new engrams are added to the germ-cell' (p. 17).

His philosophical position is not very clearly defined. While he is inclined to believe that 'in all living things there is something psychic' he also believes that 'the mnemic quality of all living things must depend on the physical changes in protoplasm'—in practice, then, the attitude of Hering and Semon, rather than that of Butler.

Looking back on the mnemic theories as a whole, we see that the idea has received two quite distinct formulations,

one psychological, the other materialistic. The root-idea, which does not achieve really adequate expression in either form of the theory, is undoubtedly a valuable and significant one; there is without question a close analogy between habit and development, and many features of development—its specificity and orderliness, its automatic character and relative independence of environment, the fact of recapitulation—receive illumination, if development be regarded as ancestral habit. The mnemic theory is the only one that gives any explanation of the historical basis of development, and it throws much light upon this important conservative element in form-production. By itself, as Semon admits (p. 14), it does not account for the progressive element in development and evolution; it requires supplementing in this respect by a Lamarckian theory of evolution, as Butler attempted to do. The transmissibility of acquired characters is necessary to the theory, and gives, as Roux has pointed out (see above, p. 108), the possibility of explaining the automatic appearance of form in advance of functioning in the first stage of development.

As we indicated at the beginning of this chapter, Butler's views both on development and on general biological method are highly original and suggestive. He made a consistent and successful attempt to treat the living thing concretely, as a real psycho-physical unity or individual, and came to grips with the big problem of the relation of the organism to its past and its future. The importance of his views will become more apparent when we consider in the next two chapters some fundamental questions of biological method.

IX

RETROSPECT. THE USE AND MISUSE OF ABSTRACTION

LOOKING back over the theories we have considered, we see that for the most part they fall into one or other of two main types. One group of theorists lays stress upon the unity of the developing organism, though not disdaining analysis; the other tends to ignore the unity of the organism and deals in terms of separate or separable characters and their presumed material representatives in the germ. The difference, though not an absolute one, is deep-rooted, and can be traced right back to the time of the Greeks, where the contrast comes out very clearly in the opposing views of Aristotle and Hippocrates; historical research would probably reveal it to be older still. Delage in his masterly survey of theories of development and heredity has already recognized a distinction between the 'organicists', as he calls them, and the 'micromerists'. The distinction which I wish to draw corresponds roughly with his, but as I look at the matter from a rather different angle, I propose to group the theories as *unity theories* and *particulate theories*.

This primary classification does not, however, sufficiently allow for the diversity of standpoint shown within the unity group, a diversity which philosophically may go very deep—as between Aristotle and Loeb, for instance. I have accordingly subdivided this group into the organismal and the physico-chemical. The organismal group of unity theories I have so named because they express in various degrees a view which we shall develop in the next chapter as the 'organismal theory' of living things. The physico-chemical group differ from the organismalists in accepting a mechanistic theory of the living thing, but they still hold to a unitary view of the organism, regarding it as a physico-chemical system. Their method is essentially physiological.

Along these lines, we can classify in the following manner the main points of view considered.

Unity Theories	Particulate Theories
A. *Organismal*	
Aristotle	Hippocrates, Democritus
Wolff	
Baer	Bonnet
Butler	Semon
Conklin	
B. *Physico-chemical*	
Delage	Weismann
Verworn	Morgan
Loeb	
Child	

One or two theories do not fit comfortably into either of the two main categories. Roux's theory, for example, is nearly, but not quite, a unity theory, and he certainly accepts in a measure the particulate conception of development. The same remark applies with even greater force to O. Hertwig, whose views we have not discussed for the very reason that he is essentially an eclectic, though with a heavy bias towards the particulate view. Another line of cleavage, which in practice, though not necessarily in theory, coincides approximately with the line we have drawn between the unity theories and the particulate theories, is that between the epigenesists and the preformationists, between those who hold that in development there is new creation of form and activity and those who regard development as a mere unfolding of what is there already, a making visible of an invisible complexity. In its fully developed form the preformationist view is always particulate, postulating a point-to-point correspondence between the germinal organization and the structure of the adult. The unity theory, on the other hand, is combined invariably with an epigenetic view of development. As we saw above (p. 29) in discussing the early preformationists and epigenesists, the one group is predominantly static and morphological in outlook, the other dynamic and physiological. Usually the preformationist

adheres to a materialistic conception of life; the epigenesist is often, but not always, a 'vitalist'.

It is not proposed at this stage to give a full analysis of the two opposing views; their characteristics will emerge as the discussion proceeds. A short recapitulation, however, of the main points brought out in the preceding chapters will be of service in orienting us with respect to them.

2. Aristotle is of course the father of the unity theory, and certain essential points are stated by him clearly and adequately. Working out his views in direct opposition to the Hippocratic theory of pangenesis, which is a typical particulate theory, he sets out the alternatives in masterly fashion. There is, in Aristotle's view, one fundamental cause of the resemblance of parent and offspring which includes the point-to-point correspondence; this is the realization of the same total functional potentialities. Hereditary resemblance is shown essentially in the functional activity of the organism as a whole, and the resemblance in minor detail is, as it were, derivative and incidental. Hereditary functional likeness is a consequence of similarity of development—of the realization of the same unified functional potentialities. Creative synthesis is then the primary cause alike of development and of heredity. It is this that brings about that 'composition' or wholeness of the body and its functions, that organic architecture and functional harmony, which make of it not an assemblage or composite of parts, but one unitary whole. The opposing particulate theory cannot account for this primary and fundamental unity of the developing organism. The semen can come only from the homogeneous parts or their elements, and not from the composition or arrangement which makes of them organs and an organism. There is therefore some primary cause of the total unitary resemblance which eludes the analytic method of the pangenesists. Development and heredity are then functions of the whole organism and are not fully explicable in terms of the activities of its parts.

Modern particulate theories attempt to account for this primary unity by assuming an architectonic complexity of

the germ-plasm, a unitary and organized structure, which corresponds in more or less detail with the structure of the developed whole, and is the ground of the unity and functional harmony of the developing organism. But this is merely to restate, in terms of a purely hypothetical material configuration, Aristotle's contention that there is one fundamental cause of the unitary functional resemblance between parent and offspring. For Aristotle's unified functional potentiality Weismann for instance substitutes the complex and organized structure of the Id, putting material preformation in place of functional potentiality. He recognizes therefore the existence of unity, but as something static.

Aristotle points out a further difficulty of the particulate theory, by remarking that if the 'seeds' (or representative particles) are different from the parts from which they come and which they make,[1] then the problem of development exists for each of the seeds, and the development of the whole is not explained by thus fragmenting it into a multiplicity of separate developmental processes.

The idea of development as a unitary process, which cannot be completely explained by analysing it into parts and stages, recurs with full force in K. E. von Baer, who maintains that one stage of development is not the sufficient cause of the next, but that all are ruled and bound up in a rhythm by the essential nature (*die Wesenheit*) of the organism to be. Contrast with this the guiding principle of W. His, some decades later, that each stage is the necessary resultant of the foregoing, and the sufficient cause of the ensuing stage.

Of the preformationists and epigenesists of the seventeenth and eighteenth centuries none is important methodologically save Bonnet, who very definitely foreshadows the Weismannian view. Darwin in 1868 revived the Hippocratic doctrine of pangenesis on a cellular basis, and Galton, by postulating a reserve stock of pangens in the germ-cells (the stirp), which is handed on from generation to generation, hit on the essential idea of the continuity of the germ-plasm.

[1] Cf. Bonnet (p. 30) and Weismann (p. 50).

The particulate view comes to full expression in Weismann. Here we have heredity explained as being due to identity, continuity, of germinal substance, and development regarded as the work of a particulate germinal organization present at the outset. All potentialities, however distant and eventual, are materialized as determinants or groups of such, quite irrespective of the occurrence of the outer events which may call them into play. The germ-plasm contains within itself material provision, in the shape of latent determinants, for all likely and even unlikely situations that may arise. One might almost say that Weismann puts the environment into the germ-plasm under the form of materialized potentialities representing eventual responses to all sorts of environmental conditions that may be encountered.

The futility of this mode of reasoning has been fully exposed by Delage, who asserts with reason that a latent character is an absent character and its hypothetical bearer or determinant a useless fiction. The fact that certain characters are separately heritable, Delage argues, does not necessarily lead to the assumption that they are represented by special determinant units in the germ, and we can get on perfectly well with a simple, non-representative 'germ-plasm', or better still with the egg-cell itself, regarded as a living organism, and as the earliest stage of the organism to be.

Development, in Delage's view, is a real formation of new organs not present in any shape before, a real differentiating out of the generalized functions of the ovum, and in this process the environment plays just as important a part as the initial germinal constitution, which must be precise and specific, but need not be complex. Delage thus approaches from a different angle the simplicity of Aristotle's conception of the unitary functional potentiality of the germ.

The physico-chemical group as a whole unite with Delage in condemning the particulate theory of development, as being otiose and misleading, and substitute the conception of the developing organism as a unitary physico-chemical system.[1] They recognize and accept accordingly the unity

[1] See also below, pp. 141–2.

of the organism, as does also in large measure W. Roux. Very important is their and Roux's insistence on the physiological process of metabolism as the foundation both of growth and of development.

The gene theory is primarily a theory of biparental inheritance, and throws little light on development. As an explanation of development it is logically less adequate than the Weismannian theory, since with its simplified germ-plasm composed of a linear arrangement of genes it tacitly ignores the problem of 'composition' and unity which Weismann attempted to meet with his architectonic germ-plasm. It tends to treat the organism as a bundle of separable characters—as a congeries, not as an organized whole.

With the mnemic theories of Hering, Butler, and Semon, there is introduced a new conception into the theory of development, that of the revival of past experience under the form of habit. Two quite distinct formulations of the idea are given, by Hering and Semon on the one hand, and by Butler on the other. The first two treat the phenomena from the materialistic standpoint, and account for mnemic phenomena on the supposition that the original stimulus leaves a material trace or engram in the substance of the organism. In Semon's hands the mnemic theory of development tends to become a particulate theory, with engrams in place of determinants. Butler on the other hand interprets the facts from the point of view of psychobiology, and accepts fully the organismal conception. Development and reproduction are for him functions of the organism as a whole; he makes no attempt to analyse them in terms of the activities of cellular and subcellular units. He holds that there is actual continuity of experience, not only within the bounds of the individual existence, but extending right back to the very dawn of life. For the material continuity of the germ-plasm he substitutes continuity of experience. In many ways his view of development is similar to Aristotle's, but he makes the great advance of realizing the historical continuity of life from its earliest beginnings. Aristotle had no idea of this immense historical background to the development of the

individual. In his view development makes a fresh start in each generation; the offspring is the child of its parents and not of its ancestors, and life is born afresh at every conception.

We have seen how this idea of the historical basis of organic activities opens up the possibility of explaining many of the principal features of development—its routine orderliness, for example, recapitulation, and anticipatory action in general.

3. We can best elucidate the contrast between the particulate and the unity theories and estimate their relative value as applied to the problems of development, if we consider the methods of *abstraction* which they respectively employ. All scientific theories necessarily abstract to a greater or less degree from the realities studied, and the character of a theory depends as much upon the mode of abstraction employed as upon the nature of the facts on which it is based. If we consider the various ways in which, for the purposes of science, abstraction is made from the living reality of the organism, we shall see how the different theories of development have arisen, and how their character has been determined by the mode of abstraction they adopt.

Biology occupies a unique and privileged position among the sciences in that its object, the living organism, is known to us not only objectively through sensory perception, but also in one case directly, as the subject of immediate experience. It is therefore possible, in this special case of one's own personal life, to take an inside view of a living organism. Naturally the direct intuitive understanding obtained by this immediate experience of living cannot form the subject-matter of biology, which is an objective science, and we must be very chary of reading into the activities of other organisms the motives and modes of experience which we discover in ourselves. Nevertheless introspective knowledge does give us an insight into the reality of the living organism which cannot be otherwise obtained, and supplies us with a standard by which to test our conceptions of the living thing.

When we conceptualize this living experience, we arrive at a definition of organism which, though it is abstract and

schematic as compared with the experienced reality, is yet rich in content as compared with the still more schematic representations commonly employed in biology. The concept of organism which we derive from a study of direct experience is that of a continuing psycho-physical unity or individuality, which acts as a whole in relation to its environment. We shall develop his 'organismal' view of the living thing in the next chapter, as the basis of our theory of development and reproduction. We shall there see that for the purposes of organismal biology it is necessary to expand this definition of organism somewhat, to bring in as essential factors the past and future of the organism and the relation of its activities to the three main ends of life—development, maintenance, and reproduction. For our present purpose however, which is to trace the steps by which for this concrete concept there come to be substituted various more abstract and restricted scientific concepts, it is sufficient to deal with the simple definition of organism, as a psycho-physical or organic unity persisting in time and acting as a whole in relation to its surroundings. 'Psycho-physical' is here used to denote that the activity of the organism is of a different order from purely physical activity. This point will be further elucidated later (pp. 172, 183–5).

4. We may distinguish two main modes of abstraction which are in practice often combined. In the first, abstraction is made from the organism as a whole, and the idea of its unity is in some measure retained. Such is the form of abstraction employed in the unity theories, and according to the degree of abstraction practised they fall into the organismal or the physico-chemical group. In the second, the mode of abstraction is analytical, and resolves the organism into an assemblage of more or less abstract parts and separate processes. This is the method which leads to the particulate view of development.

We shall deal first with abstraction applied to the organism as a whole.

As we have already seen, the first stage of abstraction from the concrete reality of organism as experienced is the concept

of organism as a psycho-physical unity or individuality. If the process of abstraction is stayed here, we get the organismal view—the view which we shall develop in the next chapter. Almost invariably the process is carried farther, and for the purposes of biology abstraction is made of the psychical aspect of living things. Our first group, however—Aristotle, Wolff, Baer, and Butler—hold the full organismal position, avoiding this abstraction of the psychical. This appears also to be the theoretical position of Conklin, though it is hardly maintained by him fully in practice. It is also the view explicitly held by Ritter and some others, whose general views we shall consider later (pp. 176 et seq.).

The second step along the path of abstraction—namely, the elimination of the psychical—is one which nowadays is almost universally taken as a matter of course. It is a step of immense importance, for it introduces at once a dualism of matter and mind, and creates between them a dividing line which can never be crossed. To reintroduce mind into living things, to reconstitute the living unity, it is necessary to have recourse to such lame expedients as psycho-physical parallelism or psycho-physical interaction, or to adopt some form of dualistic vitalism. With the psychical aspect eliminated, the organism becomes a material system, similar in nature to, though more complex in structure than, other material bodies.

The complexity and variety of organization naturally provoke investigation, and give rise on the one hand to the science of organic form, in which types of structure are distinguished and their variants classified (morphology), and on the other hand to the study of the functioning of the different types (physiology). Morphology tends to remain a formal and abstract science, until it is revivified by the study of function; physiology develops very soon the concept of the organism as a complicated mechanism. Here two somewhat diverse points of view emerge—the teleological and the dynamical.

A machine is definitely a teleological construction, and the working of its parts can be fully understood only if their

relation to one another and to the action of the whole be realized and grasped. The same view can be applied to the organism, which may be regarded as a teleological mechanism or machine, albeit of extreme complexity. The teleological point of view has undoubtedly great heuristic value in biology, and is in fact much used.

But the progress of physico-chemical study applied to the living thing has shown that the organism cannot be separated from its environment, with which it maintains the closest relations of interchange of matter and energy. Hence the conception arises of the organism as a physico-chemical system, standing in closest connexion with its physico-chemical environment. The simple concept of the organism as a formed machine is then replaced by the more general concept of it as a dynamical system. From this to the application to the organism of the general philosophical concept of material determinism there is only a step, and the organism tends then to become merged in, and hardly distinguishable from, the general flux of material events. We shall consider later the consequences of a purely materialistic treatment of living things.

It is to be noted that in both the teleological and the biochemical formulations the organism retains a considerable measure of unity—very definitely so when it is considered as a machine, and to a considerable extent also when it is regarded as a dynamical system. But both formulations are abstract as compared with the living reality of organism, or even with the primary concept of it as psycho-physical unity or individuality.

In our survey of theories we have not encountered any pure machine-theory of development, and this is easily comprehensible, for the machine-concept is primarily applicable to the formed organism, and only with great difficulty to the organism in process of formation. A machine that constructs and repairs itself is something beyond our present ken.

Of theories treating the organism in formation as a physico-chemical system we have seen several—those of Loeb and Child for example, and in considerable measure also those of

Delage and Verworn. Loeb finds the ground of the harmonious structure and unitary functioning of the organism in the fact that it is from the very beginning in the egg a unified physico-chemical system. Child, who fully realizes the fact of unity or wholeness, regards the developing organism as a reaction-system behaving as a whole. He takes the proper physiological view that structure or organization is not a cause but an effect of metabolic functioning, that the organism is a dynamical rather than a statical unity. Modern physiology teaches that the cell is a chemo-dynamic system, which requires constant oxidation to preserve its structure. 'The life machine is therefore totally unlike our ordinary mechanical machines. Its structure and organization are not static. They are in reality dynamic equilibria, which depend on oxidation for their very existence.'[1]

Delage's ultimate goal is the explanation of development in terms of its physico-chemical determinism, but he treats the organism and the cell as at least provisional unities. The importance of the cell as a natural biological unit is also stressed by Verworn.

All these physiological theories then, though abstracting completely from the psychical aspect of living things, retain in some measure the concept of the organism as a whole in regarding it as a physico-chemical system. They properly belong therefore to the unity group.

Roux's position is an interesting one. He comes very near the organismal view by his insistence on the functional activity of the living organism, and the need to state the laws of biology first in terms of elementary functions. He is, however, prevented from regarding the living thing as an organic or psycho-physical unity by his acceptance of the materialistic conception, with its elimination of the psychical. The functions or 'complex components', in terms of which he attempts to explain development, can therefore never be completely joined up to a central unity or organism in the concrete sense. Nevertheless his attempt to work with

[1] F. G. Donnan, 'The Mystery of Life' (Brit. Assoc. Address), *Nature*, vol. cxxii, 1928, p. 514.

biological rather than physico-chemical concepts is highly significant, and puts him ahead of the other physico-chemical theorists.

Turning back now to the morphological method of study, we see at once that it is by its very nature an abstract method. The morphologist concentrates on the structural aspect of living things, and regards function as derivative from structure. Contrast the physiological view which we have outlined above. Applied to development the morphological method of thought may be characterized as the kinematic, since it sees in development merely a succession of structural phases, each of which is the resultant of the last, and the cause of the ensuing, phase (cf. His, p. 95). Linked with this static or kinematic mode of abstraction, which betrays the morphological habit of thought, there is usually a strong tendency to disregard or abstract from the environment as a developmental factor. The morphological abstraction in its entirety exerts its chief influence on the theory of development when combined, as it usually is, with the analytical mode of abstraction which we shall shortly proceed to discuss. The weakness of the morphological approach to the problems of development and heredity is well brought out by D'Arcy Thompson in the following passage.

'It would seem evident', he writes, 'that, except in relation to a dynamical investigation, the mere study of cell structure has but little value of its own. That a given cell, an ovum for instance, contains this or that visible substance or structure, germinal vesicle or germinal spot, chromatin or achromatin, chromosomes or centrosomes, obviously gives no explanation of the *activities* of the cell. And in all such hypotheses as that of "pangenesis", in all the theories which attribute specific properties to micellae, idioplasts, ids, or other constituent particles of protoplasm or of the cell, we are apt to fall into the error of attributing to *matter* what is due to *energy* and is manifested in force: or, more strictly speaking, of attributing to material particles individually what is due to the energy of their collocation.... The *things* which we see in the cell are less important than the *actions* which we recognize in the cell.'[1]

[1] *On Growth and Form*, Cambridge, 1917, pp. 157–8. Cf. Child's dynamic view of organization.

Abstraction from the living reality of organism reaches of course its highest degree in the mathematical or statistical treatment of living things. Here the organism is regarded merely as a numerical value—a number, a weight, a dimension. Mathematical laws of growth, for instance, may be worked out, in which the organism is treated simply as a quantity which increases in accordance with a certain formula. Clearly such formulation gives only the most general and abstract account of the process, highly useful though it may be within strict limits.

To recapitulate the main stages of abstraction from the organism as a whole—we get from the *living reality as experienced*, which is our ultimate standard, *first*, the primary abstraction or conceptualization as *psycho-physical unity* or *individuality*, from which may be developed the organismal theory of living things, and *second*, by abstraction from this of the psychical aspect, the ordinary 'scientific' conception of the organism as a *machine*, or more generally a *physico-chemical system*. This gives us the mechanistic abstraction, which may remain however to some degree integrative, i. e. may still regard the organism as to some extent a unity. According as stress is laid on form or on functional activity, we get either a static-kinematical or a dynamical conception of the organism.

5. The use of analysis is characteristic of science generally. Given a complex body, the chemist proceeds immediately to resolve it into its elements, to determine their relative proportions, and in some cases their architectonic arrangement. The same tendency is shown very clearly in biology. Given an organism, the morphologist's first thought is to discover its structure in minutest detail, to resolve it into its constituent organs and cells and their arrangement. The same process of analysis is applied to what appears to be the ultimate vital unit, the cell; this is decomposed into its constituent parts, nucleus, cytoplasm, chromosomes, mitochondria, and so on, and each of these elements is further resolved as far as may be into smaller parts, as for instance chromomeres, linin threads, and granules of all kinds. The

process is even extended beyond the limits of microscopical vision, and hypothetical units, such as biophors, bioblasts, and genes, are freely invented to fill the gap between the just visible units and the complex colloidal molecules which make up the bulk of living matter. The method of morphological analysis leads then to a biological atomism, analogous to the atomism of the chemist.

From the physiological side also there starts a similar process of analysis or decomposition. The physiologist studies for choice isolated organs or organ-systems—the properties of a muscle-nerve preparation, for example, or the functions of the isolated heart. Even when he studies a major organ-system as a whole, the nervous system for instance, his method remains analytical; he resolves the action of the nervous system into the action of reflex arcs in their interconnexion with one another.

Another analytical method of study is to concentrate on cell-physiology, in the hope of explaining the activity of the organism as a whole in terms of the functions of its presumed ultimate units or constituents. To quote Donnan again: 'We must decompose or analyse the great mass phenomena of life into their elementary unit or constituent phenomena. To-day general physiology in its application of physics, chemistry, and physical chemistry to the living cell, is the fundamental science of life' (ibid., p. 513).

Now this analytic method, employed both in the study of form and in the study of function, is quite indispensable in biological research, and has yielded extremely valuable results. It is essential also for organismal biology. But we must note that it necessarily entails abstraction. The initial step which leads to abstractness of treatment is of course the isolation and definition of parts and part-processes as such. To define is to separate, and to separate is to ignore or to disregard in some measure the relations with other parts and with the whole. In the living thing there are in actuality no separate parts, no separate processes, for no part can be adequately characterized save in terms of its relations to the whole.

By the process of morphological analysis we can, for instance,

resolve the organism into its component cells, but the cells so distinguished are abstract morphological units, characterized statically, in terms of structure. Actually the living tissue-cell is indissolubly linked up, by reason of its functional activity, with the neighbouring cells, and, through the *milieu interne* and the nervous system, with the general activities which the whole organism is pursuing. The tissue-cell takes part in the activity of the whole, and it is dependent for its own continued existence as a living part upon its manifold functional relations with the whole. If we distinguish it as an independent unit or component we necessarily abstract from its full reality; we disregard its functional connexions or relations with the whole, and form a simplified and static conception of it.

In the living thing there *are* no completely separable or independent parts; if we distinguish separate units or components it is at the cost of artificially simplifying our definition of them by abstracting from their continuing relations with the activity of the organism as a whole. It is primarily because the parts or constituents so distinguished are to a large extent abstract that it is impossible fully to reconstitute from them the whole from which they are themselves derived by the process of analytical abstraction. This is true even if we characterize them physiologically.

Contrast in this respect a machine. The machine has separate parts; it can be taken to pieces and put together again; its parts can be adequately characterized in terms of their own structure, apart from their relations to the machine as a whole. This is not the case with the organism. Here the parts can be adequately characterized only in terms of their functional relations to the organism as a whole. These relations, which are manifold and subtle, involve time and process, a taking part or merging in the total activity of the continuing unity which is organism.

The unity of the organism is accordingly not decomposable without loss, and cannot be resynthesized in its original completeness from the abstract components distinguished by analysis. We may sum this up in the following cardinal law

of biological method: *The activity of the whole cannot be fully explained in terms of the activities of the parts isolated by analysis, and it can be the less explained the more abstract are the parts distinguished.*

Since analysis is necessary for biological science we must accept the fact that our biological results will be to a certain extent abstract and schematic, and we must strive to correct this abstractness as far as possible by distinguishing only such elements as are concrete and biological, not physico-chemical and abstract, and by carrying out as complete a reconstitution or reintegration of such elements as may be possible.

It follows from what we have said that the parts cannot be understood save in relation to the whole, and so we arrive at our second law of biological method: *No part of any living unity and no single process of any complex organic activity can be fully understood in isolation from the structure and activities of the organism as a whole.* To regard any process or structure by itself without relating it to the general activity of the organism is to deal with something which is in large measure abstract and unreal. To re-invest it with some degree of concrete reality it is necessary to re-integrate it into the whole. Its isolation by analysis should be provisional only, and after analysis there should always follow re-integration. We know that the reconstitution of the original unity will be incomplete, but we must make it as complete as possible.

The necessity for envisaging every physiological process in its relation to the activity of the organism as a whole has been fully stressed by Dr. J. S. Haldane and his followers (see below, pp. 174–6), who take up a position which is in practice, if not in theory, similar to the organismal. Even from the mechanistic standpoint, the need is recognized, by both morphologist and physiologist, for resynthesis of the parts and part-processes isolated by analysis. Both would agree that the meaning or significance of the parts and processes they isolate from the whole can be fully realized only if they are put back again in their place and seen in relation to the structure and the activity of the whole.

Clearly no part or organ lives a completely independent life, but can exist and perform its proper function only in the closest dependence on, and co-ordination with, the rest of the body. All parts and organs are, as Kant would say, reciprocally means and ends, and all co-operate in the life of the organism as a whole.

'For', as D'Arcy Thompson writes, 'the life of the body is more than the *sum* of the properties of the cells of which it is composed: as Goethe said, "Das Lebendige ist zwar in Elemente zerlegt, aber man kann es aus diesen nicht wieder zusammenstellen und beleben"' (ibid., p. 38).

I cannot forbear to quote another passage from the same author where the importance of the unitary or integrative view is most clearly brought out.

'We tend, as we analyse a thing into its parts or into its properties, to magnify these, to exaggerate their apparent independence, and to hide from ourselves (at least for a time) the essential integrity and individuality of the composite whole. We divide the body into its organs, the skeleton into its bones, as in very much the same fashion we make a subjective analysis of the mind, according to the teachings of psychology, into component factors: but we know very well that judgment and knowledge, courage or gentleness, love or fear, have no separate existence, but are somehow mere manifestations, or imaginary co-efficients, of a most complex integral' (p. 712).

So it is with the organs of the body—they form one harmonious and indissoluble whole.

'Muscle and bone, for instance, are inseparably associated and connected; they are moulded one with another; they come into being together, and act and react together. We may study them apart, but it is as a concession to our weakness and to the narrow outlook of our minds. We see, dimly perhaps, but yet with all the assurance of conviction, that between muscle and bone there can be no change in the one but it is correlated with changes in the other; that through and through they are linked in indissoluble association: that they are only separate entities in this limited and subordinate sense, that they are *parts* of a whole which, when it loses its composite integrity, ceases to exist. The biologist, as well as the philosopher, learns to recognize that the whole is not merely the sum of its parts. It is this, and much more than this. For it is not a bundle of parts, but an organization of

parts, of parts in their mutual arrangement, fitting with one another, in what Aristotle calls "a single and indivisible principle of unity"' (pp. 713–14).

That the parts can be understood only through their relations to the whole is then a cardinal principle of all sound biological thinking, and it is recognized as such by all competent thinkers.

In the foregoing discussion I have for the sake of contrast somewhat over-exaggerated the difference between the unity theories and the particulate. There is in practice no absolute antithesis between them. Even on the particulate conception the unity of the organism cannot be completely ignored, and we have seen how Weismann for example implicitly recognized it in his concept of the Id as an organized unit. No one would nowadays seriously maintain that the organism is merely a bundle or assemblage of unit characters; the existence of 'composition', arrangement, organization, unity, can simply not be disregarded. On the other hand, even the organismalist, though firmly convinced that the unity of the living thing cannot be completely explained in terms of the activity of its parts, will not hesitate to make use of the method of analysis in the practical conduct of his researches. He will employ the method of analytical abstraction where necessary, remaining conscious of its limitations, and seeking always to reintegrate into the activity of the whole the partial activities which he distinguishes.

This very difficult but fundamental question of the relation of the parts to the whole, which I have treated rather inadequately and abstractly above, will be further considered in the next chapter, where an attempt is made to work out a more adequate concept of organism, taking account of the all-important *temporal* relations of organic activity. The life of an organism is essentially a unitary functional or dynamical process, in which 'whole' and 'parts' are inextricably interconnected. Both whole and parts are together the expression of the life of the individual.

6. So far we have considered the legitimate use of the analytical method, the inevitable abstractness of which can

be to some extent mitigated by reintegration. There is, however, a misuse of the analytical or disintegrative method which leads to disastrous consequences, many of which we have seen in our survey of theories of development.

There is, for example, a tendency on the part of some authors to neglect the natural biological unities of organism and cell and to speak of 'living substance' as if it were a self-existent thing. Actually life, so far as observation goes, exists only in the form of individual units, and 'living substance' is therefore a pure abstraction, to which nothing corresponds in Nature. The process of abstraction, of elimination, is here carried too far; essential elements are left out, and the result is a purely fictional concept. A further misuse of this already abstract concept is to speak of a 'germinal substance', as Weismann and so many others do. It is true that Weismann means by this something more than mere substance, namely the complex architecture of the Id, but even in this form his germinal substance is something quite abstract and unsubstantial.

More dangerous still is the misuse of the method of morphological analysis. The organism is by this method resolved into cells, cells into their constituent parts, and the substance of the cell into hypothetical units, to which are attributed many of the essential vital functions. This fractionalization is a method of approach to the problems of heredity and development which has become traditional and habitual, so that nowadays any other way of looking at these problems is rarely considered, and it is of course the basal method underlying all particulate theories. It is generally, though not invariably, coupled with the idea that some at least of these ultimate units represent and give rise to, or at the least co-operate in the formation of, particular parts or characters of the organism. This idea of representative particles is, we have seen, a very old one, dating back at least to the Greeks, and revived again by Bonnet, Darwin, and Weismann. It derives some of its force and verisimilitude from the fact that certain characters appear to behave as units in inheritance—a particular lock of white hair, for

example, may recur from one generation to another. From facts of this kind it is easy, but illogical, to conclude that all characters of the organism are separable in inheritance, that the organism is, as it were, a bundle of separate characters, represented separately in the germ, which can be shuffled about, so that some of the offspring get one set, some another, and so on indefinitely.[1] It may be remarked that to distinguish separate characters at all in the organism has necessarily something artificial and abstract about it (see above, p. 77). Obviously the number of characters that can be distinguished is infinite, but yet none of them is in reality separate from the rest. The lock of hair, for instance, clearly cannot arise apart from the organism which manifests it. Separate or separable characters are therefore to a very large extent abstractions. But the idea that the organism is a composite of separate characters, each of which is represented in the germ by a separate vital unit, seems to have a perennial fascination for the human mind.

There are two points to be distinguished in considering the resolution of the cell into ultimate vital units. The first is that the procedure is logical enough so far as the actual existence of discrete units is concerned. Microscopical analysis reveals in the cell the existence of smaller and smaller discrete units; there is no reason to believe that the limits of microscopic or ultra-microscopic vision coincide with the limits of discreteness of living matter; physical chemistry leads us to think that the ultimate basis of living protoplasm is a colloidal solution in which are found dispersed

[1] Cf. C. E. McClung: 'If the germ cells are, then, a register of racial experience, it is clear that a mechanism for assorting and recombining the pages of this story would tend to an ultimate uniformity of expression with almost all degrees of individual variation. Such possibilities seem to lie within the nature of the chromosome behavior in maturation and fertilisation. The haploid group of either parent cell contains the full register of class characteristics, and, upon fertilisation, the individual is provided with a double record. In its germ cells the double pages are separated and assorted by chance into different units, so that, if there are but eighteen of these pages in the single series, the possible varieties of it are 262,144. When later fertilisation combines these in duplicate, the possible expressions of variation reach the incomprehensible number of 68,719,736.' In Cowdry, *General Cytology*, Chicago, 1924.

particles of molecular size. Hence it is quite possible, and even likely, that ultramicroscopic units exist, intermediate in size between visible granules and colloidal particles. Brücke and Herbert Spencer long ago arrived at this conclusion on theoretical grounds. The conception of the cell as built up of ultimate and invisible living units is widespread among modern biologists.[1] O. Hertwig resolves the cell into bioblasts, M. Heidenhain into protomers, Weismann into biophors, de Vries into pangens, and so on. Hertwig's bioblasts, for example, are the ultimate vital units that possess the power of assimilation, growth, and division. They cannot be further split up without losing these distinctively vital properties.

'Just as plants and animals can be resolved into thousands and thousands of cells,' writes Hertwig,[2] 'so also the cell itself is built up of numerous elementary vital units, which lie below the limits of microscopical visibility, are different from one another chemically, and form here the cytoplasm and its numerous differentiation-products, there the nucleus, the nuclear membrane, the linin threads, the chromosomes, the trophoplasts and so on, and as integral parts of an organism stand in organic relations with one another. "As physics and chemistry go back to molecules and atoms, so must the biological sciences penetrate down to these units, in order to explain from their inter-relations the phenomena of the organic world" (De Vries).'

So far, so good; these hypothetical units are arrived at by an extension of the legitimate method of analysis that led to the formulation of the cell-theory; the procedure is logical, though it leads to further abstractness.

The real mischief begins when these hypothetical units are regarded as the sole hereditary elements, and as the formative agents in development. The train of reasoning which leads to this conclusion runs somewhat as follows. It is axiomatic, the theorists assert, that the male and the female contribute equally to the heritage of the offspring. The only equivalent structure in the male and the female gamete is the nucleus. The nucleus must therefore carry all

[1] It does not however find favour with modern physiologists, cf. F. G. Hopkins, *Nature*, xcii, 1913, p. 220.

[2] *Allgemeine Biologie*, 6th and 7th edit., Jena, 1923, p. 65.

the hereditary characters, and the nuclear substance must be the controlling and differentiating agent in development. Further, it must be of an extremely complex organization, since we must suppose it to contain the material representation of each separate character of the organism. If it contains particles representative of all the characters, these must be of ultra-microscopic size, else there would not be room for them in such a minute object as the chromatin head of a spermatozoon. We are led therefore to the conception of a complex germinal or nuclear architecture built up of ultra-microscopical units—the biophors of Weismann, the pangens of de Vries, or what other names may suit the fancy. They correspond in fact, though not necessarily in ascribed function, to the physiological units distinguished by structural analysis pushed to its theoretical limit.

This conception of an architectonic and formative germ-plasm is of course most fully developed by Weismann, and has been considerably modified and softened down in more recent days. Weismann, however, with de Vries (as well as those who believe in the *real* existence of genes as particulate bodies), does undoubtedly attribute to these ultimate vital units amazing powers of determining and differentiating the characters of the developing organism. We have already pointed out in dealing with Weismann's theory that he ascribes to the action of his biophors and determinants, which are 'parts' of the cell, effects which in reality result from the functional activity of the cell or the organism as a whole. There is introduced therefore a curious dualism or opposition between the active formative agent and the matter acted upon. This dualism is already evident in Darwin's theory of pangenesis, where the germ-cell is to all intents inert until activated by the entrance of the pangens—it is the soil waiting for the seed, Aristotle's germinal 'material' waiting for the sensitive soul to be supplied by the semen of the male. In de Vries' theory, also, just as in Weismann's, the cytoplasm is regarded as material to be acted upon and transformed by the pangens or determinants, issuing from the nucleus like a swarm of workers intent on

their task. Here we re-encounter that analogy between the germ-plasm considered as an active agent, controlling the metabolic processes of the cell, and the immaterial entelechy of Driesch, upon which we have already remarked (see above, pp. 50 and 102). The germ-plasm is, as it were, a material entelechy. The attempt to find an internal formative mechanism as the cause alike of heredity and development, which is characteristic of nearly all modern theories, results necessarily in this separation of agent and material, just as the attempt of the vitalists to reintroduce life into the mechanistic abstraction that stands for organism results in a dualism or opposition between the immaterial agent and the material mechanism which it in some way controls. In either case one arrives at a *Deus in machina*.[1]

The nuclear organization, the germ-plasm, or the gene-complex of modern theories, is accordingly invested with semi-magical powers of control. To show that this is no exaggerated statement, let me quote the words of a recent author: 'Taken together, the chromosomes represent the sum total of all the elements of control over the processes of metabolism, irritability, contractility, reproduction, &c., that are involved in the life of an organism, but in the measure that organisms differ, so do the natures of their controlling mechanisms.'[2]

How is this truly astonishing conclusion arrived at? By misuse of the method of analytical abstraction. We note first of all that the point of view is essentially morphological. In dealing with development abstraction is made of function and environment; the ordinary physiological functions of the cell and the organism are left out of the picture entirely.

The organism is regarded as a collocation of subordinate parts, of units of diverse degree, but the problem of 'composition', organization, or wholeness is ignored, and attention

[1] One may call this curious inversion of the problem the *fallacy of reduplication*, in order to indicate the fact that the functional manifestations of the whole are assumed to be due to an internal mechanism, or entelechy, or agent, which as it were doubles the role.

[2] C. E. McClung, 'The Chromosome Theory of Heredity', in Cowdry, *General Cytology*, Chicago, 1924, p. 634.

is concentrated on the lowest grade of these units, the biophors, bioblasts, pangens, or what not. These are supposed to represent the parts or the characters of the developed organism, and in some way, which always remains mysterious, to give rise to them in the course of development. (The hereditary units being the purest of abstractions, it is of course natural that their relations with the characters they determine should remain obscure.)

Hereditary units and 'determinants' of all kinds are pure abstractions; the process of analysis has been carried so far that it is impossible to reconstitute from these purely abstract elements the activities of the cell or the organism as a whole. All that is left then to the theorists is to smuggle back into the determinants or other 'parts' the powers and functions which belong rightly to the organism as a whole, and have inevitably been dropped out during the process of analysis. The concept of the organism as a whole, which has been destroyed by unrestrained analysis, is reintroduced surreptitiously, and the qualities and powers of the organism as a whole attributed to certain abstract and subordinate *parts* of it, just as to entelechy are ascribed powers and capabilities which properly belong only to the whole organism.

The result of this method of approach is the unnecessary complication of an already sufficiently difficult problem. The particulate type of theory substitutes for the relatively simple visible facts of development an excessively complicated re-description of them in terms of an organization of purely abstract and fictional elements, which it locates within the nucleus—as it were, an invisible and active organism or agent within the visible organism. The inadmissibility of all particulate theories from the standpoint of a dynamical or physiological treatment of development has been fully and adequately demonstrated by Delage and Child, but to emphasize the point I may quote a particularly clear summing-up by J. A. Ryder.[1] His general standpoint is that

[1] 'A Dynamical Hypothesis of Inheritance', *Wood's Holl Biological Lectures for 1894*, Boston, 1895, pp. 23–53.

'metabolism is . . . the sole agent in effecting the mechanical and dynamical rearrangement or sorting of the molecules into organs during development'. He writes:

'Specially endowed corpuscles or "biophors" are not only needless as conditioning form or function, but also out of the question, dynamically considered. No creature can be supposed to have its life or germinal properties associated only with certain corpuscles within it, since we cannot suppose an organized whole dominated by a portion of it; it is not possible, for example, to conceive of individual life except from the entire organism that manifests it. There can be no "biophors"—bearers of life—the whole organism must do that as an indivisible unit' (p. 52).

The physiological point of view could not be more clearly expressed.

The organismal attitude is similar, and has been stated by Ritter[1] as follows:

'According to the organismal conception, all life phenomena, including those of inheritance, consist in the activities and inter-activities of an enormous number of substances and units and forces, all of which, in exhaustive analysis, are dependent upon the organism as a living whole. It is, therefore, as futile to hunt in one corner as another for the physical basis of heredity in an exclusive and more or less metaphysical sense.'

7. In the above discussion the type of theory criticized is the pure particulate theory, which assumes in greater or less degree a point-to-point correspondence and causal connexion between the units of the germinal architecture and the parts or characters of the developed organism. More modern theories, such as the theory of the gene, are not quite so schematic and crude, and the idea of 'determinant' in the full Weismannian sense has now become practically obsolete. The supremacy of the nucleus is still fully maintained, but the chromosomes and their constituent elements, the genes, are regarded more as conditioning than as determining the characters of the organism; their action is differential rather than fully determinative. It is probable that the physiological interpretation of the gene hypothesis is not far

[1] W. E. Ritter, *The Unity of the Organism*, Boston, 1919, ii, p. 33.

distant, when the gene will cease to be regarded as a self-existent particulate unit and will be merged in the general physiological activity of the nucleus. But the gene theory in its original formulation, where genes are treated as real entities, is tainted with the same faults as the particulate theory of Weismann—the resolution of the organic unity into isolated parts or characters, the opposition of the nuclear substance as active and formative to the cytoplasm as comparatively inert material, the invention of purely abstract and fictive units or parts endowed with mysterious formative powers. So long as the gene is regarded as a purely hypothetical concept invented for the specific purpose of explaining certain complicated facts of inheritance, no great harm is done. But when it is treated as a real existent body all the factitious and gratuitous complications of the particulate theory tend to set in. The hypothesis is accordingly one to be employed with the greatest circumspection.

In particular the idea of nuclear dominance, which it shares with the older particulate theories, appears abstract and non-physiological. From the point of view of physiology the relations between nucleus and cytoplasm are obviously complex, intimate, and ever-changing. There cannot be any absolute separation between the functions of the nucleus on the one hand and the functions of the cytoplasm on the other. Their relations are reciprocal, each affecting each in constant succession. Nor can either be understood save in relation to the other, and to the activity of the cell as a whole, for neither is capable of long-continued existence apart from the rest of the cell. To establish then a rigid distinction between the nucleus and the cytoplasm, to allot to each element clearly defined and separate functions, is to deal with unreal abstractions. To regard one as controlling the other is quite illegitimate and introduces that dualism of agent and thing acted upon which runs through and vitiates all theories of nuclear dominance.

8. We have hitherto touched very lightly upon the philosophies underlying the various theories of development and heredity of which we have treated. We have found it

more important to discuss the actual methods of attack upon the problems which have been adopted, and we have traced how by the use and misuse of abstraction certain of these theories get farther and farther away from the living reality.

It is very curious how the same types of theory recur throughout the ages. The contrast between the unity theory and the particulate is fully developed among the Greeks, who also, as is well known, foreshadowed some other 'modern' scientific conceptions, as for instance the theory of evolution. This would seem to indicate that certain types of explanation are natural to the human mind, and that the diversity shown arises not so much from the facts, with which the ancients were singularly ill-acquainted, as from some fundamental diversity of mind. Some men are organismalists by nature, others take naturally to the particulate view. It would seem that man creates science in his own image, and that different types of mind create different kinds of science.

There are also underlying this initial diversity of standpoint other differences arising from the particular philosophy consciously or unconsciously adopted. Aristotle, for instance, holds very special philosophical views of his own, which are quite different from those of modern times, and his constructive theory of development is, as we have seen, thoroughly imbued with his particular philosophy. The preformationists were believers in the principle of mechanism introduced in their time by Descartes and the early physicists, and they took refuge in the theory of preformation because a mechanistic explanation of epigenesis appeared to them impossible. The epigenesists did not accept this way out of the dilemma, and frankly embraced vitalistic views.

K. E. von Baer was a believer in a sort of universal vitalism, and was ready to regard matter and spirit as alike human abstractions from the living reality. He also was an epigenesist.

When we come to the modern theories we find that, with some few exceptions, they are based upon the materialistic conception of reality. In a book to which we shall often have occasion to refer in the succeeding chapter, Whitehead

enunciates the following valuable maxim: 'When you are criticizing the philosophy of an epoch, do not chiefly direct your attention to those intellectual positions which its exponents feel it necessary explicitly to defend. There will be some fundamental assumptions which adherents of all the variant systems within the epoch unconsciously presuppose. Such assumptions appear so obvious that people do not know what they are assuming, because no other way of putting things has ever occurred to them.'[1] This is particularly true of most modern theories of development, for they are based upon a materialistic philosophy which is by their authors accepted without question or inquiry, and as a matter of course. To most biologists, the existence of the germ-plasm, for example, appears axiomatic and unquestionable; actually the concept of germ-plasm is derivative from the materialistic philosophy, and has only this restricted and relative value.

The domination in modern times of a materialistic or mechanistic basal philosophy is obvious in the physico-chemical or physiological theories; it is equally clear in the germ-plasm and gene theories, and W. Roux, though in practice getting somewhat beyond the materialistic method, yet bases his theoretical views directly upon the mechanistic philosophy, as being the only sound foundation of exact science. Butler is of course a definite exception, with his psycho-biological interpretation of development and evolution, but the other mnemists, Hering, Semon, and Francis Darwin, have not shaken free of the materialistic notion of physical traces or engrams, and remain wedded to a form of biological atomism.

The materialistic theory of reality is nowadays somewhat *vieux jeu*, and has been very considerably shaken and modified by the new views of the constitution of matter and the establishment of the principle of relativity. It is, however, in its classical Laplacean form that it influenced and still influences biological method. This classical materialism may be defined as the belief that all physical phenomena, including the phenomena of life, are in ultimate analysis the

[1] A. N. Whitehead, *Science and the Modern World*, Cambridge, 1926, p. 61.

outcome of the motion of material particles, that such material particles are bound up in rigidly determined spatial systems or configurations, the successive stages of which follow one another in time according to immutable law, the position and acceleration of each particle being completely conditioned or determined by the immediately antecedent states of the changing configuration which is reality. The progression of events as perceived by the senses is merely the outward show of this incessant movement of invisible and ultimate particles.

It is a conception singularly ill-adapted to explain heredity and development, for as Picard writes, 'Classical mechanics has led to types of differential relations, by postulating, more or less explicitly, a principle of non-heredity, according to which the infinitesimal changes that occur in a system depend solely upon the present state of that system.'[1]

It is under the influence of this mechanistic schematism, accepted as the true and only foundation of science, that the biologist proceeds at once and without hesitation to carry out that decisive abstraction of which we have spoken above—the elimination of the psychical. This done, he can treat the living thing as a complex mechanism—as a machine, or as a physico-chemical system, or, theoretically at least, as an artificially isolated section of the general configuration flux. In practice, we may remark in passing, he is often not consistent in his materialism, for he switches back on occasions to the primary organismal view, as when he ascribes to living things perceptions and feelings, or uses concepts such as development, heredity, or regeneration, which are essentially biological.

The effect on his theory of development of such acceptance of mechanistic principles is very obvious. This is why he clings to the conception of germ-plasm as the ground of heredity and the causal agent of development. It is the nearest he can get to a configurational explanation of these phenomena. If the development of a particular kind of organism starts out from a particular material organization,

[1] In *De la Méthode dans les Sciences*, 2nd edit., Paris, 1910, p. 25.

the germ-plasm of the species, and if this germ-plasm is reproduced or continued unchanged to form the starting-point of the next generation, then hereditary resemblance is satisfactorily explained on mechanistic principles. If development is due to the formative influence of the germ-plasm it is understandable that it follows the same general course from one generation to another in any normal environment.[1] Actually the germ-plasm is a completely abstract and hypothetical substance, and the explanation offered of development and heredity is equally abstract and formal. The concept of germ-plasm is derivative from a mechanistic philosophy and has no other justification. It is, as we have seen, arrived at in the particulate theories by way of biological atomism, but the fundamental background is the mechanistic philosophy.

With the mechanistic scheme the concept of potentiality is incompatible; it is for this reason that Weismann, for example, disregards the plain evidence of the senses that development is an actual new creation of form and an actualization of functional potentialities, and postulates instead an initial material complexity which simplifies itself in the course of development, inverting thus the true sequence of events. The mechanistic philosophy can take no account of the historical aspect of vital activity; it must assume that past history is summed up in the present constitution of the germ-plasm.[2]

It is for this reason that mechanists like Semon postulate in the germ-plasm material traces or engrams to represent in the present the past experience of the race. Engrams materialize the past, just as representative particles or determinants materialize the future (cf. Delage, p. 81 above).

As we shall see in more detail in the next chapter, an organismal theory, which makes no abstraction of the psychical aspect but regards the living thing as a 'psycho-

[1] Logically, he should include environment as part of the primary configuration.

[2] Cf. McClung: '. . . the germ cells are old and strongly established in their characters—the resultants of millions of years of repeated experiences which are registered in their structure'. 1924, p. 650.

physical' or organic whole, manifesting a distinctive kind of activity which is different from that of inorganic units (and may therefore properly be called 'organic'), offers a better line of approach to the problems of development and heredity, and holds out hope of a less abstract and more adequate treatment of these problems. It will enable us to deal more satisfactorily with the all-important temporal relations of organic activity, to regard the living thing as a real continuing unity, extending through time. For the abstract concept of germ-plasm it will substitute the more concrete conception of the ovum as itself an organism—the future organism in its simplest state—having the elementary powers and functions of an organism, and the potentiality of developing the physical and psychical capabilities of the adult.

X

THE ORGANISMAL POINT OF VIEW

MATERIALISM as a philosophical doctrine has long been dead, and as a scientific method its limitations are now becoming apparent. Even in their application to physics, in which field they originated and won their most striking triumphs, the simple mechanistic principles are proving inadequate in face of the new facts and the new conceptions.

'The progress of science', writes Whitehead,[1] 'has now reached a turning point. The stable foundations of physics have broken up: also for the first time physiology is asserting itself as an effective body of knowledge, as distinct from a scrap-heap. The old foundations of scientific thought are becoming unintelligible. Time, space, matter, material, ether, electricity, mechanism, organism, configuration, pattern, function, all require reinterpretation. What is the sense of talking about a mechanical explanation when you do not know what you mean by mechanics?'

Or again,

'The appeal to mechanism on behalf of biology was in its origin an appeal to the well-attested self-consistent physical concepts as expressing the basis of all natural phenomena. But at present there is no such system of concepts' (ibid., p. 129).

The fact is that biology, impressed by the success of physical concepts in their own sphere at the time of the great development of the classical mechanics, took over to itself concepts and methods which were clearly inappropriate and inadequate to the new subject. Now these concepts are found to be unsatisfactory even in their original sphere; in particular, the configuration idea has gone, and with it the old Laplacean conception of universal material determinism.[2]

[1] A. N. Whitehead, *Science and the Modern World*, Cambridge, 1926, p. 21.

[2] Cf. Professor A. S. Eddington: 'On the scientific side, a new situation has arisen. It is a consequence of the advent of the quantum theory that *physics is no longer pledged to a scheme of deterministic law.* Determinism has dropped out altogether in the latest formulations of theoretical physics and it is at least open to doubt whether it will ever be brought back. . . . The future is a combination of the causal influence of the past, together with unpredictable elements—unpredictable not merely

The philosophical foundations of mechanistic biology have crumbled away.

2. What we have to do then is to look round for a new set of concepts which will enable us to establish biology on a footing of its own. These new concepts must of course link up with those of the new physics on the one hand and with psychological principles on the other. The task is not a simple one, considering that neither physics nor psychology has yet come to any settled agreement regarding its own guiding ideas.

It is particularly in connexion with studies of the developing organism that we feel the need of special biological concepts, for the adult and finished organism may be regarded from the point of view of physiology as approximating sufficiently nearly to a mechanism to be treated as such, provided the principle of wholeness or unity be recognized. The same is, however, not true of the developing organism, as Sir Charles Sherrington has pointed out in his Presidential Address to the British Association in 1922.

'Of not a few of the processes of the living body,' he writes, 'such as muscular contraction, the circulation of the blood, the respiratory intake and output by the lungs, the nervous impulse and its journeyings, we may fairly feel, from what we know of them already, that further application of physics and chemistry will furnish a competent key. . . . Turning to other aspects of animal mechanism such as the shaping of the animal body, the conspiring of its structural units to compass later functional ends, the predetermination of specific growth from egg to adult, the predetermined natural term of existence, these and their intimate mechanism, we are, it seems to me, despite many brilliant enquiries and enquirers, still at a loss to understand.' [1]

because it is impracticable to obtain the data of prediction, but because no data connected causally with our experience exist.' *The Nature of the Physical World*, Cambridge, 1929, p. 294.

[1] Cf. Claude Bernard: 'Il y a dans un phénomène vital, comme dans tout autre phénomène naturel, deux ordres de causes: d'abord une cause première, créatrice, législative et *directrice* de la vie, et inaccessible à nos connaissances, ensuite une cause prochaine ou *exécutive* du phénomène vital qui toujours est de nature physico-chimique et tombe dans le domaine de l'expérimentateur. La cause première de la vie donne l'évolution ou la *création de la machine* organisée; mais la machine, une fois créée, fonctionne en vertu des propriétés de ses éléments constituants et sous l'in-

Nor are mechanistic concepts really applicable to many of the broader problems of general biology—problems of adaptation, of behaviour, of the factors of evolution. From a strictly mechanistic point of view there *is* no adaptation, there *is* no behaviour—there is only a series of material configurations in course of transformation. So-called mechanistic theories of evolution have been from time to time propounded on the basis of random variation and chance selection, but these are neither factually nor logically sound, and carefully ignore most of the obvious features of the process which they purport to explain.

3. The vitalistic solution of the problem of biological method offered by Driesch cannot be accepted as really satisfactory, for the reason that it does not lead to any distinctively new method of attack. It is, in practice, materialism plus an entelechy—abstraction of the psychical has taken place. The critical and destructive side of Driesch's work is admirable; his system of philosophy merits the most careful study; but his entelechy is of no *practical* use as a biological concept.[1]

4. The proper alternative to the mechanistic method in biology is in a sense obvious and lies on the surface. It is suggested by ordinary commonsense acceptance of the plain facts without abstraction, and it is in effect used by biologists to a very great extent, whatever their theoretical views may be. Common observation shows us that vital activities are manifested by *individuals*, whether unicellular or multicellular. Even from the point of view of structure, life is not a property of any substance, however complex, but of an organization. The idea of 'living substance' is, as we have seen, a pure abstraction, to which nothing corresponds in Nature. The ascription to sub-cellular and abstract vital units such as biophors and determinants of the full properties of life is likewise inadmissible. The lowest unit that

fluence des conditions physico-chimiques qui agissent sur eux.' *La Science expérimentale*, Paris, 1890, pp. 53–4.

[1] For a fuller treatment of Driesch's views see *The Study of Living Things*, 1924, pp. 20–6.

shows the full range of vital activities and is independently viable is the cell-organism, whether in an elementary form with scattered chromatin, as in some bacteria and algae, or in a more evolved form with definite distinction of nucleus and cytoplasm. This statement may require some modification when more is known of ultra-microscopic, filter-passing 'organisms', but proof of their independent life seems still to be lacking.[1]

From the point of view of function, the unique character of the living individual as the fundamental unit of biology stands out unmistakably, for the individual is essentially a functional unity, whose activities are co-ordinated and directed towards the development, maintenance, and reproduction of the form and modes of action typical of the species to which it belongs. To quote Sherrington again: '. . . the living creature is fundamentally a unity. In trying to make the "how" of an animal existence intelligible to our imperfect knowledge, we have, for purposes of study, to separate its whole into part-aspects and part-mechanisms, but that separation is artificial. It is as a whole, a single entity, that the animal, or for that matter the plant, is finally and essentially to be envisaged.'[2]

There is an interesting parallel in an old Address by St. George Mivart:

'But as each living creature is a highly complex unity—both a unity of body and also a unity of force, or a synthesis of activities—it seems to me', he writes, 'that we require a distinct kind of physiology to be devoted to the investigation of such syntheses of activities as exist in each kind of living creature. I mean to say that just as we have a physiology devoted to the several activities of the several organs, so we need a physiology specially directed to the physiology of the living body considered as one whole, that is, to the power which is the function, so to speak, of that whole, and of which the whole body in its totality is the organ. In a word, we need a *physiology of the individual*.'[3]

[1] See A. E. Boycott, 'The transition from Live to Dead: the Nature of Filtrable Viruses', *Proc. Roy. Soc. Medicine*, xxii (Path.), pp. 55–69, 1928.

[2] Presidential Address to the British Association, 1922.

[3] Address to the British Association, 1879. Reprinted in *Essays and Criticisms*, vol. ii, London, 1892. See p. 223.

The importance of the unity of the developing individual is stressed also by Claude Bernard, who writes: 'En disant que la vie est l'idée directrice ou la *force évolutive* de l'être, nous exprimons simplement l'idée d'une unité dans la succession de tous les changements morphologiques et chimiques accomplis par le germe depuis l'origine jusqu'à la fin de la vie' (1890, p. 430).

As to the facts there can be no difference of opinion; the obvious conclusion to be drawn is that biology should be the science of individual living organisms.

This is in practice, as we have said, recognized by most biologists; they deal in the course of their work with organisms as units, and necessarily employ expressions and concepts which relate specifically to organisms and are not applicable to inorganic objects. 'As a matter of fact,' writes MacBride in an article on Vitalism, 'the ordinary biologist, however materialistic he may profess himself in theory, does not in practice avail himself of the "machine comparisons" in order to explain the activities of living beings, but takes such biological concepts as "stimulus", "reaction", and "adaptability"—which are certainly neither physical nor chemical ideas—as the building stones of the theories which he constructs.'[1] This being the case, need we look farther for the biological principles we require? That biology is essentially the study of living individuals is common ground. Can we not, from this starting-point, develop the principles of an autonomous biology?

5. Everything depends of course upon what conception we form of 'organism'. If we take 'organism' in a general sense as being merely a provisional concept, and straightway proceed to abstract from the psychical aspect and to treat the living thing as being only a complicated mechanism, if we go on to analyse its activities into part-aspects and part-processes which are necessarily abstract, we fall back into the analytic and materialistic interpretation. It is true that even on this interpretation there would still be room for provisional generalizations, having the value of temporary

[1] *Scientia*, July 1922, p. 23 of the separate copy.

biological laws.[1] W. Roux for instance regarded the establishment of the general functions or modes of action of living cells and tissues (his 'complex components') as a necessary preliminary to the complete analysis of these modes of action into their simple or physico-chemical components, but such laws would be superseded as soon as the physico-chemical determinism was discovered of the processes they described. There is, however—and this is the essential point—no need for biology to be limited by the materialistic postulates; it is perfectly possible to frame a working conception of organism which shall be less abstract than that of mechanism and shall do less violence to the essential facts.

6. Let us see if we can formulate such a conception. In the first place, the functional unity of the living thing must be emphasized. The activities of the parts work together for the good of the whole; the meaning of any functional activity can be understood only if its relation to the activity of the whole is known. It is not really possible to study adequately any one function, e.g. excretion, without taking into account its relations to other functions and conditions, as assimilation, circulation, the composition of the internal medium, and so on, and without determining what part it plays in the economy of the whole. This teleological conception can, however, be applied also to a machine; this also is a unity, in which each part has a definite role to play in relation to the functioning of the machine as a whole. But as we saw in the last chapter (pp. 146–9), a machine can properly be analysed into constituent and independent parts, whereas in the living organism separate parts can be distinguished only by the artifice of abstraction, and its unity is not decomposable without loss. The organism differs from the machine also in another respect, in that all its functions are directed to one or other of three great ends, namely the development of specific form and activities, the maintenance or restoration of such typical form and activities, and the reproduction of

[1] I took this point of view in 1911, in an article on 'Vitalism' in *Scientia* (*Rivista di Scienza*), ix. 320–45.

specific type. None of these broad characteristics of living things is shared by any machine.

We must therefore add to our first point—that the organism is a functional unity—the further characteristic that the functional activities of the living thing are essentially related to the ends of development, maintenance, and reproduction. Implied in this fuller definition are certain temporal relations of vital activities which are fundamental for our conception of organism. The organism is *not*, like a machine, a static construction, but a constantly changing organization of functional activities, which tends towards some end, and in such tendency is influenced by its past. Its activity is related both to its past and to its future.

That these are not vague general assertions made to bolster up a preconceived notion of the organism is made clear if we consider fairly and with an open mind the general activities of living things. That in development there is a definite progression to an end or goal, i.e. a reference to the future, cannot be denied. That the course of development is essentially influenced by the past history of the race is likewise difficult to deny, and we sum up such facts of the historical background of development in the laws of heredity and recapitulation. The reference to past and future is clear also in all cases of restitution or regeneration, and it is so obvious in behaviour as to need no pointing out. Reproduction too is essentially a preparation for the future, and its course is determined and defined by what, for want of a better word, one might call the organic tradition handed down by countless ancestors.

Let it be made quite clear that this reference to past and future is not necessarily or usually (so far as we know) a conscious reference on the part of the organism. It is, for example, necessary for description and understanding of the bald facts that we use the word 'end' in considering the phenomena of development, but it is not implied that the developing organism is conscious of the end or purpose which appears *to us* to be embodied in its development. Whether the organism makes conscious reference to the past and the

future is really a point of minor importance; what *is* important to realize is that organic activities are objectively of such a character that we cannot fully understand them unless we consider them in relation both to the past and to the future of the organism.[1] The question as to what underlies this apparent reference behind and before in vital activities—whether it is conscious effort, as Samuel Butler was disposed to believe, or unconscious striving, as others think—is hardly one for biology, but rather for philosophy, to decide. That something does underlie it, that there is some real ground for the objective purposiveness of living things, is all we need postulate for our new biology.

We include then in our concept of organism the characteristic that vital activities have a reference to the future of the organism and are influenced in their course by the past history of the organism and of its ancestors. Exactly how this reference is effected by the organism itself, or even whether it is effected by the organism *qua* individual, we can leave unsettled at least for the present, but on the point that for an understanding of its vital activities we must consider both the past and the future of the organism there should be no difference of opinion. When in an embryo there is formed an eye long before it can function, when we see the germ-cells segregated early and slowly coming to maturity, when we watch the mother-bird building a nest for eggs that are not yet laid, we must, if we are to understand these actions at all, take into consideration their essential reference to the future. When we see in the development of the frog the

[1] A striking example of 'prospective reference' is afforded by certain types of cleavage, especially in teloblastic division. 'In all such cases', writes Wilson (1925, p. 1005), 'we cannot comprehend the specific forms of cleavage without reference to the end-result of the formative process; and the problems here encountered cannot be separated from those of development in the larger sense. The teleological aspect of cleavage thus suggested has been recognized more or less clearly, by many observers; most adequately perhaps by Lillie, who has urged that with this principle in mind "one can thus go over every detail of the cleavage, and knowing the fate of the cells, can explain all the irregularities and peculiarities displayed". The egg is not merely a cell dividing as best it may under the stress of simple and obviously mechanical conditions. It is "a builder which lays one stone here, another there, each of which is placed with reference to future development" (Lillie)'. On cleavage as 'reminiscent' of past conditions, see Wilson, p. 1011.

reproduction of stages passed through by its ancestors near and remote, the formation and destruction of organs which had significance in some distant past and now have none, when we see the mature eel setting forth on its dangerous journey to spawn thousands of miles away in the depths of the Atlantic, we must in accounting for these facts bear in mind their essential relation to the past history of the race; they can be understood only on the hypothesis that in some way or other the past of the organism and of its ancestors still influences its present activities.

Time then enters as an essential element into our definition of organism. The living thing at any one moment of its history must be regarded as merely a phase of a life-cycle. It is the whole cycle that is the life of the individual, and this cycle is indissolubly linked with previous life-cycles—those of its ancestors right back to the dawn of life. This is what we mean by the continuity of life. And the activities of the organism at any stage of its career can be understood only if they are re-integrated in the individual and the evolutionary life-cycles.

7. There is yet another characteristic to add to our concept of organism before it can be regarded as reasonably complete, and that is a characteristic belonging to the functions and activities themselves. The actions of the organism as a whole, regarded from one point of view, are extremely complex, in that they appear to be compounded of a multitude of actions of lower order. Every behaviour-action of a Metazoon, for example, entails the functioning of a neuro-muscular mechanism of some complexity, which functioning is made up of the activities of the component sensory, nerve, and muscle cells. The activities of the cells might in their turn, it would seem, be analysed into their physico-chemical components. Any action of the whole organism would appear then to be susceptible of analysis to an indefinite degree—and this is in general the aim of the physiologist, to analyse, to decompose into their elementary processes the broad activities and functions of the organism.

But it is obvious that by such a procedure something is lost, for the action of the whole has a certain unifiedness and

completeness which is left out of account in the process of analysis (see above, pp. 145–9). This unifiedness of response can best be illustrated by reference to one's own experience of living—one's actions for example in playing tennis are unified responses of one's whole physical and mental being at the time, and an analysis of them into their constituents would inevitably miss out the essential point, namely their accurate co-ordination and applicability to the situation arising. In our conception of the organism we must then take account of the unifiedness and wholeness of its activities. This is the more necessary since we have seen that the activities of the organism all have reference to one or other of three great ends, and that both the past and the future enter into their determination. Such characteristics can belong only to actions possessing a concrete reality which is not wholly exhausted by analysis into constituent elements or parts.

If this view be accepted, it follows that the activities of the organism as a whole are to be regarded as of a different order from physico-chemical reactions, both in themselves and for the purposes of our understanding. The relation of the whole-action of the organism to the processes underlying it and to purely physico-chemical action will be considered in more detail at a later stage in this discussion. Meantime we shall add to our definition of organism that the actions of the whole have a unique character and unity which renders them irreducible to processes of lower order. We may here recall our law of biological method that the whole cannot be completely explained in terms of its parts (p. 147 above).

It follows from this proposition that in so studying the responses of living things we do not regard them as purely physico-chemical; we are in fact precluded from treating them as being wholly such. Our definition of whole-action is sufficiently wide and general to cover actions which by common consent are called psycho-physical—as for instance the behaviour of man and the higher animals. We shall see later that in many respects, though not in all, the 'organic' activities of living things—those manifested through growth and differentiation—resemble behaviour-actions.

We have now sketched, in the very broadest outline, a conception of organism which is completely free from any mechanistic assumption, and seems on the face of it to fit the main facts reasonably well. Let us summarize our conclusions. We agree that biology is essentially the study of individual living organisms, that the individual organism, whether unicellular or multicellular, is the unit to which all biological concepts and laws must relate. The organism is essentially a *continuing* unity, and all its activities are directed towards the ends of development, maintenance, and reproduction; these have reference to the future and to the past of the organism, and cannot be understood unless these temporal relations are taken into account; its activities have a certain unifiedness and wholeness which makes them irreducible to processes of lower order; the action of the organism as a whole is therefore not completely explicable in terms of the actions of the parts, and still less in terms of physical and chemical action.

On these principles, which appear to be consonant with the broad facts of observation, it is clearly possible to build up a biology free from the materialistic limitations which have hampered its development hitherto.

8. There are several ways of arriving at the principles of an autonomous biology similar to those which we have just outlined. There is first of all the way we have taken here—to start from conceptions which are tacitly followed by most biologists (I except biochemists!) in the practical conduct of their researches, and, accepting the broad facts of observation at their face value, to generalize these without paying much attention to ultimate questions of philosophy. We acquire thus a provisional concept of the organism which gives us certain principles for biology, the final test of which must lie in their success or failure in practice.

The conception of the organism as essentially a unified whole is of course a very old one. It was clearly stated by Aristotle, and Kant has formulated it at great length in the *Critique of Judgment*. Coming to modern times, Driesch has developed the idea fully in his *Ordnungslehre* (1912,

2nd edit., 1923), and has added the new category of 'Individuality' or 'Wholeness' to the Kantian list. Ungerer has applied the conception in the botanical field in his book *Die Regulationen der Pflanzen* (1919, 2nd edit., 1926). Many other references might be given.[1]

A fruitful line of advance has been that taken by Dr. J. S. Haldane, who has clearly distinguished the concepts of mechanism, organism, and personality—starting out, one imagines, from a Hegelian point of view—and has applied the methods of his 'New Physiology' with great success in his classical studies on respiration.[2] The following quotations may give a sufficiently good idea of his views.

'The fundamental facts with regard to life do not fit into the conceptions by means of which we at present interpret inorganic phenomena. Life is something which the biologist as such must treat as a primary reality, and no mere artefact. . . . The ground hypothesis or conception is that each detail of organic structure, composition, and activity is a manifestation or expression of the life of the organism regarded as a separate and persistent whole' (1917, p. 100).

Conscious personality is, however, more than organism and requires for its study other concepts than the purely biological; there is accordingly a hierarchy of concepts from the psychological down through the biological to the physico-chemical.

'Although a man is a person and not a mere organism, we cannot trace personality throughout all, or nearly all, of what we observe in a man. To interpret the details as best we can, we have to fall back on the conception of life in the biological sense, just as in details of what we observe in connection with living organisms we have to fall back on ordinary physical and chemical interpretations' (ibid., p. 115).

[1] See particularly H. Höffding, *Der Totalitätsbegriff*, Leipzig, 1917, and *Erkenntnistheorie und Lebensauffassung*, Leipzig, 1926. Also C. G. Joh. Petersen, 'On Some Biological Principles', *Kgl. Danske Vidensk. Selskab, Biol. Meddel.*, vii. 2, Copenhagen, 1928.

[2] *Mechanism, Life and Personality*, London, 1913; *Organism and Environment as illustrated by the Physiology of Breathing*, New Haven, 1917; *The New Physiology*, London, 1919; 'The Relations between Biology and Psychology', Aristotelian Soc., Suppl. vol., 1923, pp. 56–75; 'The Fundamental Conceptions of Biology', *Brit. Med. Journ.*, March 3rd, 1923; *The Sciences and Philosophy* (Gifford Lectures, 1927–8), London, 1929.

Haldane lays great stress on the importance of normality in the environment, both external and internal. His attitude is essentially that of a physiologist freed from the mechanistic trammels. His views are very similar to those developed here, but they differ in some important respects, notably in the more definite separation of psychology from biology; organic activities are in his view uninfluenced by past experience, and the organism is moved merely by 'blind immediacy'.

Haldane's 'biological' conception of living things is beginning to exercise a considerable influence on physiological thinking. Thus Pembrey fully accepts Haldane's position when he writes:

'The physiological unit is the living organism, whether it is a single cell, such as an amoeba, or a complex of millions of cells, such as a man. Physiology deals with living processes which cannot be described in anatomical terms, or even in the terms of chemistry and physics: it is a branch of biology, and must be described in biological language. The most important influence in the return to biological conceptions in physiology in this country has been the work and teaching of Haldane.'[1]

The importance from the physiological standpoint of keeping the organism as a whole in view has been emphasized also by C. G. Douglas in his address to the Physiology Section of the British Association in 1927.[2] 'The more we examine the normal behaviour of the body', he writes, 'the more is it brought home to us that the maintenance of the natural life and integrity of the organism depends on the closest co-ordination of all its different parts; all the organs are interdependent, and can have no real existence save as active components of a corporate whole' (p. 846). Accordingly, 'in physiology the organism as such, be it man or one of the lower animals, is our unit, and whatever methods we may employ in our investigations, we must keep that essential fact before us' (p. 846). Or again, 'Unless we deliberately study

[1] M. S. Pembrey, 'Physiology', in *Evolution in the Light of Modern Knowledge*, London, 1925, p. 264.

[2] 'The Development of Human Physiology', *Nature*, Dec. 10, 1927. See also C. Lovatt Evans's address to the Physiology Section, Brit. Assoc., 1928.

the normal organism in its entirety, I do not see how we can gain any adequate conception about what is really implied by life' (p. 846).

In 1919 the American zoologist W. E. Ritter published an important book[1] contrasting the 'organismal' with the 'elemental' theory of the organism—a distinction corresponding almost exactly with that drawn in our last chapter between the unity or organismal and the particulate view. The word 'organismal' I have in fact borrowed from Ritter. He subjects the elementalist conception of the organism to very complete and penetrating criticism, particularly in its relation to the theory of development, and in its place he puts the view that the organism as a whole, considered as organism and not as mere mechanism, is the fundamental concept in biology to which all others must be subordinated. His central idea is that 'The organism in its totality is as essential to an explanation of the elements as its elements are to an explanation of the organism' (i, p. 24). The organism 'taken alive and whole' is the primary unit for biology; 'living substance' is a myth, for 'All the living substance that has existed on this earth or anywhere else has existed through and in and because of individual living beings' (i, p. 115). A separate function or part-process, e.g. a reflex act, cannot be understood save 'by considering it in the light of the organism's entire complex of normal activities; i.e., in accordance with the conception of the organism as a whole' (ii, p. 184).

Ritter's organismal conception of the living thing implies no dualistic vitalism:

'Ideas, or psychoids, or entelechies, or "principles" of any kind conceived as independent of, or even separable from, sensible objects are quite as repugnant to me, an organismalist, as they are to any elementalist. The essence of my contention is that the natural substitute for these imponderable things are the *living, individual organisms themselves*, and not the particles of which they are composed.

[1] *The Unity of the Organism, or the Organismal Conception of Life*, 2 vols., Boston, 1919. See also Ritter and Baily, 'The Organismal Conception. Its Place in Science and its Bearing on Philosophy', *Univ. California Public. Zool.*, xxx, pp. 307–58, 1928.

Each and every individual organism is a natural reality by exactly the same criteria that the atoms, molecules, cells, and tissues of which it is composed are natural realities' (ii, p. 149).

The organism is then a natural unity manifesting activities *sui generis*, which are of a different order from those manifested by inorganic objects. We cannot draw a hard and fast distinction between those of an organism's activities that appear to be 'physical' and such as appear to be 'psychical'—all should be regarded as 'vital' or 'organic'.

'If in all the world there is such a thing as objective truth, what we start with and have ever to deal with in studying psychic phenomena, just as in studying all other phenomena of animals, are individual objects or bodies of very particular construction and activity. And by no possibility can consistent thought and statement avoid acknowledging that that vast assemblage of acts and other manifestations which are called psychical are yet only part and parcel of the still vaster assemblage of acts and manifestations presented by the very same living objects, that is, by organisms. Our occupation will be basally with an *object*, some particular organism, having innumerable attributes, which being classified fall rather roughly into two great groups, one of which we name physical or material and the other psychical or spiritual. . . . Our discussion, then, will never lose sight of the fact that the acts with which we deal are acts of the *organism* and not of any of its parts merely, whether these be conceived as material or psychical. No matter how far particular acts may be dependent upon, and so explicable by, particular parts, this dependence cannot in reality be the whole story, for the sufficient reason that the parts are, finally, non-existent except as derivatives of and dependencies upon the organism' (ii, p. 215).

It will be seen that Ritter's point of view is essentially the same as that taken here, though he has arrived at it by a different route. I take this opportunity of acknowledging my indebtedness to Ritter, though I read his book at a comparatively late stage in the development of the ideas set forth in this volume.

My own line of approach, if the personal note may be permitted, was from a position of 'methodological vitalism' (1911) in which I questioned the adequacy of mechanistic explanations to cope with the problem of the 'composition'

and co-ordination of organic activities, through a phase of psychobiology, in which I emphasized the importance of the psychical aspect of living things, pointing out that even 'organic' activities such as growth-responses had many of the objective characteristics of behaviour-action, to my present position, in which psychological notions play a less prominent part (see below, pp. 190–2). For the sake of completeness a short account of the psychobiological point of view, as I developed it,[1] may be given here. The line of attack consists in starting out from the facts of immediate experience—unifiedness of personality, undividedness of the perception-response relation—and arguing that some measure at least of such essentially psychological unity must pervade all the activities of living things. It follows from these premises that the concept of organism cannot be based on physico-chemical mechanism, but must necessarily take account of the psychophysical unity or individuality of living things. A few quotations in illustration of the psychobiological point of view may perhaps be allowed me.

'Vital activity is a thing which though directly experienced by each one of us cannot be fully conceptualized or explained by analogy with any other form of activity. We know it best and most intimately under the form of behaviour—of muscular action expressing conation and guided by perception—but there is no reason to suppose that it differs essentially in its less explicit, less conscious modes. In any case, our own experience is the only standard and exemplar of vital activity that we have, and we must, whether we will or no, conceive all other psychical or vital activity upon this model' (1924, pp. 61–2).

Again,

'The relation—perception, hormé, response—is unique and fundamental, and cannot be translated into terms of another order. The living thing is not a machine, for it shows persistent and prospective

[1] 'Psychobiology', *Proc. Aristotelian Soc.*, 1922–3, pp. 141–56; 'The Relations between Biology and Psychology', *Aristot. Soc.*, Suppl. vol., 1923, pp. 76–85; *The Study of Living Things*, London, 1924. For another presentation of the psychobiological point of view, see A. Wagner, *Vorlesungen über Tier- und Pflanzenkunde*, Leipzig, 1912. *Das Zweckgesetz in der Natur*, München und Leipzig, 1923, and *Die Vernunft der Pflanzen*, Dresden, 1925. Also W. Mackenzie, *Alle Fonti della Vita* Genoa, 1912.

tendency or striving, and its responses are adjustable to a wide range of circumstances. It is not a mechanism actuated by a psyche, for this formulation simply pushes the mystery further back, by ascribing to an immaterial agent or element of nature the faculties and powers of the organism as a whole. The living thing is not the clay moulded by the potter, nor the harp played upon by the musician. It is the clay modelling itself, or as Aristotle puts it in a beautiful figure, being moulded directly by Nature herself, without the aid of tools "but, as it were, with her own hands"' (ibid., pp. 60–1).

We shall see more clearly later that the concept of organism which we are working out here does include essential elements derived from the psychobiological view.

Another line of thought which converges in practice to similar conclusions regarding the method of studying living things, and opens up the possibility of an autonomous biology freed from at least some of the mechanistic assumptions, is the doctrine of emergence, which has been developed from the philosophical side particularly by Professor S. Alexander,[1] and in its application to biology expecially by Professor C. Lloyd Morgan.[2]

9. For our special purpose here—the elaboration of a concept of organism adapted to the study of development—the most valuable philosophical contribution of recent years is, however, that made by Professor A. N. Whitehead, in a series of important books,[3] particularly in his *Science and the Modern World*. He propounds in the book referred to a theory of 'organic mechanism' which is of the highest interest and importance for biology. The doctrine which he maintains is, 'that the whole concept of materialism only applies to very abstract

[1] *Space, Time and Deity*, 2 vols., 2nd edit., London, 1928.

[2] *Emergent Evolution*, London, 1923; *Life, Mind and Spirit*, London, 1926; 'Biology' in *Evolution in the Light of Modern Knowledge*, London, 1925; 'A Concept of the Organism, Emergent and Resultant', *Aristot. Soc. Proc.*, 1926–7, pp. 144–76. See also C. D. Broad, *The Mind and its Place in Nature*, 1925, and Symposium (E. S. Russell, C. R. Morris, and W. Leslie Mackenzie) on the Notion of Emergence, *Aristot. Soc.*, Suppl. vol., 1926.

General Smuts's well-known book *Holism and Evolution* (London, 1926) develops generally this same conception of the emergence of 'wholes' in cosmic evolution.

[3] *An Enquiry concerning the Principles of Natural Knowledge*, Cambridge, 1919; *The Concept of Nature*, Cambridge, 1920; *Science and the Modern World*, Cambridge, 1926, New Impression, 1927; *Process and Reality*, 1929.

entities, the products of logical discernment. The concrete enduring entities are organisms, so that the plan of the *whole* influences the very characters of the various subordinate organisms which enter into it. In the case of an animal, the mental states enter into the plan of the total organism and thus modify the plans of the successive subordinate organisms until the ultimate smallest organisms, such as electrons, are reached. Thus an electron within a living body is different from an electron outside it, by reason of the plan of the body. The electron blindly runs either within or without the body; but it runs within the body in accordance with its characters within the body; that is to say, in accordance with the general plan of the body, and this plan includes the mental state. But the principle of modification is perfectly general throughout nature, and represents no property peculiar to living bodies' (1927, pp. 98–9).

Whitehead bases his whole philosophy of nature on the concept of organism, as being much more concrete than the abstract ideas of matter and mind, and he defines it in such a wide way as to make it apply to all unities in nature, from the living thing down to the electron. He regards their modes of action as not being mechanically determined in the sense of the classical materialism, and he allows for mental states as influencing the general 'plan' of the living organism. This conception of organism is developed from a standpoint which is practically the same as that from which the psychobiologist sets out, for individual living experience is taken to be the ultimate standard of reality.

'In this sketch of an analysis more concrete than that of the scientific scheme of thought', he writes, 'I have started from our own psychological field, as it stands for our cognition. I take it for what it claims to be: the self-knowledge of our bodily event. I mean the total event, and not the inspection of the details of the body. This self-knowledge discloses a prehensive unification of modal presences of entities beyond itself. I generalize by the use of the principle that this total bodily event is on the same level as all other events, except for an unusual complexity and stability of inherent pattern. The strength of the theory of materialistic mechanism has been the demand, that no arbitrary breaks be introduced into nature, to eke out the collapse of an explanation. I accept this principle. But if you start from the immediate facts of our psychological experience, as surely an em-

piricist should begin, you are at once led to the organic conception of nature' (ibid., pp. 91–2).

This quotation may not be altogether clear without a knowledge of Whitehead's nomenclature, but the general purport is perfectly plain. He turns the tables completely on the materialist, and instead of attempting to explain nature from below upwards, with the help of a few highly abstract concepts, he takes the problem by the other end and generalizes the concrete idea of organism, as given in immediate experience, so that it applies right down the scale, from the organic to the inorganic in its minutest details. All unities that we meet with in the world of nature are organisms, albeit of different degree. 'The character of existent reality is composed of organisms enduring through the flux of things. The low type of organisms have achieved a self-identity dominating their whole physical life. Electrons, molecules, crystals, belong to this type. They exhibit a massive and complete sameness. In the higher types, where life appears, there is greater complexity' (pp. 250–1). This doctrine of a hierarchy of 'organisms' is, as we shall see, of great assistance to us in understanding the relation to the whole of the various subordinate individualities in the living body, and the relation generally of physico-chemical action to organic activity.

It follows on Whitehead's view that the inorganic world, as it is presented to our senses, is for the most part a series of aggregates of the lower ('inorganic') organisms, and 'the characteristic laws of inorganic matter are mainly the statistical averages resulting from confused aggregates. So far are they from throwing light on the ultimate nature of things, that they blur and obliterate the individual characters of the individual organisms. If we wish to throw light upon the facts relating to organisms, we must study either the individual molecules and electrons, or the individual living beings. In between we find comparative confusion' (p. 139). The theory of evolution in particular forces the organic conception of nature upon us.

'Evolution, on the materialistic theory, is reduced to the role of

being another word for the description of the changes of the external relations between portions of matter. There is nothing to evolve, because one set of external relations is as good as any other set of external relations. There can merely be change, purposeless and unprogressive. But the whole point of the modern doctrine is the evolution of the complex organisms from antecedent states of less complex organisms. The doctrine thus cries aloud for a conception of organism as fundamental for nature. It also requires an underlying activity—a substantial activity—expressing itself in individual embodiments, and evolving in achievements of organism. The organism is a unit of emergent value, a real fusion of the characters of eternal objects, emerging for its own sake. Thus in the process of analysing the character of nature in itself, we find that the emergence of organisms depends on a selective activity which is akin to purpose. The point is that the enduring organisms are now the outcome of evolution; and that, beyond these organisms, there is nothing else that endures. On the materialistic theory, there is material—such as matter or electricity—which endures. On the organic theory, the only endurances are structures of activity, and the structures are evolved' (p. 135).

10. In our general sketch of a conception of the living organism which should be the basis of a new biology freed from the materialistic assumptions, we did not probe very deeply into the relations between the activity of the organism as a whole, or the activities of its parts, and the physico-chemical processes which in some way form the basis or foundation of vital activity in general. It is necessary now to consider this point in more detail.

The problem has always been a difficult one for any theory of an autonomous biology. So long as one is dealing with living unities as independent wholes, the position is clear enough and the principles we have worked out above can be applied. But when or if one attempts to analyse the activities of a vital unity into its constituent elements, one is immediately brought up against (1) the problem of the relation of the parts to the whole, and (2) the more general problem of the relation of vital activity to physico-chemical process. The first we have partially discussed in the preceding chapter and it will occupy us again in the chapters which follow. As regards the more general problem, we saw reason

above to conclude that vital activities could not be completely analysed into their physico-chemical constituents, that in the process of analysis something is dropped out and the essential unity of organic action left unexplained. This conclusion remains perfectly valid, but the general question requires further consideration. What for instance should be the relation between the results of our proposed organismal method and those of biochemistry? The biochemist frankly treats the living thing in its physico-chemical aspect only, but his method is a perfectly legitimate and fruitful one. We must try to connect up the organismal method with the biochemical in some rational way.

The danger for biology here has always been to fall into a dualism of the physical and the psychical, of means and agent, of mechanism and entelechy. If, when the activities of the organic unity are analysed into physico-chemical part-processes, there is always something left unaccounted for, some 'surd' element, one is very apt to hypostatize this into an active agent of some kind—an entelechy, a psychical factor, or the like—which in some way uses and modifies the physico-chemical processes of the organism, just as in synthesizing a new compound the chemist intervenes to regulate the reactions in view of the desired end. But such a conception is clearly inadmissible; it is arrived at by abstracting from the living unity those properties that distinguish it from an inorganic aggregate, and investing these properties with a hypothetical entity on which is thrown the onus of organizing physico-chemical processes into vital actions.[1] It leads to an irremediable dualism.

The real solution of the problem is, I think, that given us by Whitehead. If, as he maintains, the materialistic conception is an abstraction applicable to Nature only under severe limitations; if the real elements in Nature are organisms of various degrees, from the living thing down to the atom; if their modes of action are never purely mechanical in the sense of the classical materialism; then the apparent dualisms

[1] Cf. the similar train of thought which leads to the postulation of the 'materialistic entelechy', the germ-plasm.

which have continually troubled the philosophical biologist disappear—dualism of mind and matter, of the 'vital principle' and physico-chemical processes—and we have instead the more manageable problem of the relations to one another of the different grades of 'organisms' forming the hierarchy of Nature. Of these, living things are clearly marked off by their special modes of activity, and of this activity we cannot say that it is either physical or psychical—it is distinctively 'vital' or 'organic'.[1]

Living things are, clearly, to use Whitehead's phrase, 'organisms of organisms'. They are compounded of separate organs, which have a certain degree of independence but are bent essentially on the service of the whole; the organs are composed of cells, which may have a considerable measure of functional autonomy, and might rank therefore as organisms of the second degree.[2] The cells in their turn have organs, or distinguishable parts different as to function, and these, though no longer capable of independent life and no longer showing the full range of vital activities, have definite functional capabilities not shared by units of lower degree; the nucleus, for example, has *in situ* powers of assimilation and growth; we might recognize therefore as 'organisms' of the third degree such semi-independent intra-cellular units as the nucleus and its parts, Golgi bodies, plastids, mitochondria and the like.[3] Below these organized and visible units there come the various grades of 'inorganic' organisms, as crystals, molecules, atoms, and electrons. The point is that there is nowhere an absolute break, there is no absolute division between the organic and the inorganic, nor between actions into which 'mind' enters and actions which are purely 'physical'. And for us the continuity must be regarded as one from above downwards; it is impossible to explain the

[1] It is this characteristic of the activity of living things which we have attempted to express hitherto by using the somewhat misleading word 'psycho-physical' (see above, p. 139).

[2] How far the cell may be regarded as an independent unity will be discussed in Chapters XI–XII.

[3] One must bear in mind that all these subordinate organic 'unities' are to a large extent abstractions.

modes of action of any one grade of unities by the modes of action of any lower grade; on the contrary, something of the character of the higher grades, as it were, filters down and colours the action of even the lowest grades. It is important to note that the sub-organismal units are organized and arranged so as to form the individual living thing, which is made of them plus their 'composition', to use Aristotle's term. For this, if for no other reason, it is impossible fully to explain the global activity of the whole in terms of the activities of its subordinate and necessarily abstract unities.

On a previous occasion[1] I proposed a classification of vital phenomena into *responses*, *functions*, and *material conditions*, including the physico-chemical *properties* of living matter. My 'responses' were the activities of the organism as a whole, 'functions' the activities of the parts, and 'properties' the action of the physico-chemical constituents of the organism. This classification requires very little modification to fit the organic conception of things which we have taken over from Whitehead. Generalizing the classification, I should prefer to speak now of the *modes of action* of unities of different degree —instead of 'responses' to speak of 'modes of action of the organism as a whole', instead of 'function' to speak of 'modes of action of organs and cells'. I should insert a separate category of modes of action of intra-cellular units, and for convenience keep the old terms of properties and material conditions, these being re-defined as the modes of action of inorganic unities within and without the organism, respectively.

It is not proposed at this stage of the discussion to enter into an analysis of the actual relations between the different grades of unities concerned in the functioning of the living organism; this will occupy our attention in the succeeding chapters. But, as we have already seen, one thing is abundantly clear—that the modes of action of lower unities do not 'cause' or fully account for the modes of action of higher; their role is rather to *condition* these higher modes, both to limit them and to render them possible.

To take a few simple illustrations—a frog or a bird cannot

[1] *Study of Living Things*, 1924, pp. 100 ff.

carry out its breeding behaviour without a neuromuscular apparatus, and this apparatus will not function unless the nerve-cells and muscle-cells are capable of exhibiting their proper modes of action. The activities of the nerve-cells and muscle-cells are necessary conditions of the whole action, but they are not in any full sense its cause. They enable the action to be carried out, and they limit at the same time the possibilities of the action. They are in a sense the *means* of the action, but means is a dangerous word to use, for it introduces a dualism of action, since it implies an active agent and more or less passive material. Putting the matter in another way, a knowledge of the nature of muscular and nervous action would not enable us fully to interpret behaviour. The typical or proper modes of action of the cells are in their turn dependent upon, but not entirely caused by, the physico-chemical processes taking place in the course of their action. The relation of these processes to the whole-action of the cell is again one of enabling and limiting, that is to say of conditioning, rather than of causing. The relation of environmental factors, whether of the external or the internal environment, to the modes of action of the cells or the whole organism, is a particularly clear instance of the general rule that the lower unities condition but do not fully account for the modes of action of the higher. The developing sea-urchin's egg, for example, as Herbst's classical researches have shown, is dependent upon a host of physico-chemical conditions for normal development. In the absence of chlorine it will not segment at all; if the sulphuric acid radical is missing the gut will not develop normally. It requires these and many other 'enabling' conditions for normal development. There are also many 'limiting' conditions of environment which the developing organism may not transgress under pain of death—limits of temperature, for instance. But though development is thus hedged about with conditions, these conditions do not in the least explain the course which development takes, nor why a sea-urchin develops from a sea-urchin's egg.

With regard to intra-cellular units, we shall see in a later

chapter (XIV, pp. 279–83) that the chromosomes, for example, may condition and modify the developmental processes of the organism, but cannot through their action in any full sense account for development and heredity.

Summing up, we may say that the activities of lower unities are to be regarded as 'means' in relation to, or as modifiers or conditions of, the activity of the higher unities which they compose, or of which they form the environment. They are to be interpreted always in relation to the activity of the organism as a whole. We must bear in mind too that the subordinate unities which we distinguish by analysis have something abstract and artificial about them, since in distinguishing them as parts we necessarily disregard many of their relations to the whole.

11. Coming back to our question as to the relation between bio-chemistry and organismal biology, we can now answer that bio-chemistry studies essentially the *conditions* of action of cells and organisms, while organismal biology attempts to study the actual modes of action of whole organisms, regarded as conditioned by, but irreducible to, the modes of action of lower unities. Put in another way, bio-chemistry in practice studies the modes of action of the lower unities, both within the organism as actual constituents of the living unit, or as forming part of the *milieu interne*, and outside the organism, as forming its external environment. Bio-chemistry deals chiefly with the products of organic activity, and if it tackles the living unities themselves it is constrained to treat them *qua* 'living substance', abstracting from the unifiedness or wholeness of the activities which they manifest. Organismal biology commences at the other end from bio-chemistry—with the study of the whole actions of organic unities, and it works down from the organism to its constituent parts, not upwards from the parts to the whole. It makes use of course of the analytical method, but bears always in mind the need to re-integrate the parts into the whole. It retains its independent status as the study of modes of action of organic unities considered in relation to their conditioning factors (action of lower unities, i.e. organic

parts, and physico-chemical processes) and to the main ends of the organism (development, maintenance, and reproduction). Bio-chemistry continues downward the study of the conditioning factors, and the two methods dovetail into each other.

On the other hand, at the opposite end of the scale, organismal biology merges easily into comparative psychology, so soon as the modes of action of the whole reach such a level as to give clear evidence of having reference to a perceived environment, when the organism must be regarded not merely as organism, but as percipient organism. Such is the case certainly with the higher insects and vertebrates and probably also much farther down the scale of beings. Organismal biology therefore appears to fit comfortably in between the psychological sciences on the one hand and the physical on the other.

12. It follows from our definition of the aims of organismal biology that its primary task is to study the modes of action of organic unities; it must not seek to resolve them completely into modes of action appertaining to unities of lower degree, though it may and should study these lower unities in their aspect of conditioning, co-operating and modifying factors. It must then deal with the fundamental functions of living individuals as its irreducible elements of explanation, and not seek to compound these out of properties belonging to unities of lower order. It will accordingly work with, and in terms of, such biological functions as assimilation, respiration, excretion, growth, differentiation, mnemic retention, perception (if the facts demand it), and response, as its fundamental elements, and will eschew the attempt to analyse these into their constituent part-processes, leaving this task to the bio-chemists.

Organismal biology will accordingly require a whole set of concepts and methods, different from those which are current in the physical sciences, and in part analogous to those employed in psychology. Its concepts must have reference to the individual organism, and not at all to abstractions like 'living substance', the 'organic machine', or hypothetical

entities like biophors: they must be able to take account of the forward-looking and backward-looking aspects of vital activities. All its laws must be stated in terms of organic unities, regarded as individuals persisting in time, whose activities are related both to the past and to the future.

Many of the necessary concepts we shall find already in use by biologists, especially of the older and sounder tradition, but they require for the most part accurate re-statement, and freeing from any tinge of materialism that may still cling to them. Certain general concepts which are often rather loosely used, such as 'function', 'cause', 'potentiality', 'conditioning', 'determining', will also require careful analysis and definition. We shall not attempt the task here.[1]

13. We cannot claim for organismal biology anything like complete adequacy, or a close approach to full understanding of the living thing. The full secret of life will always elude a purely scientific treatment; it may be experienced, imagined, and felt, but never completely pinned down and explained. Something will always escape definition and measurement. Nevertheless we may rightly claim that the organismal method gives us a biology less remote from the truth than the abstract and schematic account to which the materialistic assumptions would limit us. It gives us a unitary biology, in which the abstractness and excessive analysis of the materialistic method are avoided; it allows us to look upon the living thing as a functional unity, disregarding the separation of matter and mind, and to realize how all its activities—activities of the whole, and activities of the parts, right down to intra-cellular unities—subserve in co-operation with one another the primary ends of development, maintenance, and reproduction.

In the materialistic scheme there is no room for such concepts. Mechanism with its unrestrained use of the method of analytical abstraction means the disintegration of the organism into a concatenation of processes of lower order, to the arrangement and collaboration of which, to their orderliness

[1] Valuable work has been done in this direction by J. H. Woodger, in his *Biological Principles*, London, 1929.

in space and time, it can supply no key. Such analysis leaves always an unknown surd, which is hypostatized as an entelechy or as a materialistic 'controlling' agent, such as the germ-plasm. The mechanistic method can study only the *conditions* of vital functioning; the specifically organic modes of action of the higher unities, cells and organisms, dissolve away in its hands into a tangle of physico-chemical processes. The organismal method, on the other hand, accepts the fact of unity and does not try to analyse organic activity completely into factors of lower order. It regards the organism not as purely material, in the sense of being merely a structural configuration, nor as a body plus a soul or entelechy, but as a unity *sui generis*, having ways of action which are not fully explicable in terms of mechanism, nor for the most part in terms of psychology, which are therefore distinctively 'organic'.

14. A word as to the relation of the organismal to the psychobiological point of view, which is based upon a particular philosophy. From the standpoint of psychobiology the organism is regarded as a monad, somewhat in Leibniz's sense, and its modes of action as being essentially of the same nature as the perception-response relation which is characteristic of conscious behaviour. This point of view certainly emphasizes one factor which it is important to realize in the formulation of the organismal method, namely that the concept of organism in the functional sense is in the long run derived from an analogy with our own conscious life as experienced. Only in immediate experience have we direct knowledge of what a living organism is, and any adequate concept of individuality, of organism, which we may form must ultimately draw upon this experience, and have reference to this experience, as the ultimate standard. The psychobiological point of view is certainly applicable to the study of animal behaviour—of response to a sensed environment by means of bodily movement—and it opens up the possibility of tracing out through the animal kingdom the evolution of the separate worlds of perception in which as monads all animals live distinct from one another, each mirroring its

own little corner of the universe and attending to such elements in it as are important for its welfare. It is applicable in all cases where the organism must be regarded as percipient. Whether and how far the psychobiological point of view may be profitably extended to the study of such activities as metabolism, growth, differentiation, and the like, is much more doubtful, and can only be decided by trial.[1] Clearly one must not apply psychological concepts unless the facts absolutely demand them, but on the other hand their use must not be excluded. One must remember that there are other forms of perception besides the perception of external relations—interoceptive perception, for example. It may be that growth-responses, such as the regeneration of lost parts, which take place under the control of the organism as a whole are mediated by interoceptive sensations. Wherever perception enters, be it even in rudimentary form, a psychobiological interpretation is called for.

It may be well to emphasize again the point that from the organismal standpoint there is no separation of vital activities into 'physical' and 'psychical'—all are organic. All actions of the organism as a whole show certain characteristics—unity, reference to past and future, adaptability—whether they are behaviour-actions or growth-actions. They must be treated then as irreducible to processes of lower order. Of these actions, a certain class require for their adequate interpretation the assumption that the organism performing them is percipient: such actions demand therefore a psychobiological interpretation, employing concepts borrowed from psychology. These are in general behaviour-actions, but the possibility must not be absolutely excluded that morphogenetic activities also may in some cases require a psychobiological interpretation.

In connexion with this question of applying psychological concepts to biological facts, it is worth while remembering

[1] I tried to make clear even in my *Study of Living Things* that 'once we leave the domain of animal behaviour, psychology is not going to help us in the study of organic responses', but this point has been generally missed even by sympathetic and understanding readers.

that the existence of consciousness in other organisms is always a matter of inference, and is not susceptible of proof. But the point is really irrelevant. In judging whether such and such actions are 'psychological', we consider whether they belong to the general type of actions known to us in immediate experience as psychical, but which even in experience are not always or necessarily conscious. We cannot use 'consciousness' as an explanation in biology.

15. In conclusion, it may be useful to apply in a preliminary way the ideas we have worked out above to the problems of development and heredity which were briefly characterized in Chapter I. In the succeeding chapters of this book certain of these applications will be considered in more detail, though no attempt will be made to work out a complete theory of development on organismal lines. For this the time is not yet ripe; all that can be done at present is to indicate some obvious lines of attack upon these problems.

The biological principles which we have provisionally adopted can be used (1) for criticism, and (2) for construction. Employed as an instrument of criticism, they enable us to make a clean sweep of certain ideas regarding development and heredity which general acceptance has rendered almost sacrosanct, namely the germ-plasm theory in all its forms, including all theories of representative particles and all theories relying upon the configuration idea. We shall reject *a limine* all particulate theories of development.

If we hold fast to the principle that the whole cannot be completely explained in terms of its parts, that the modes of action of higher unities may be conditioned, but cannot be fully accounted for, by the modes of action of lower unities, it follows that no substance and no sub-cellular unities can be invoked as sufficiently accounting for the phenomena of development and heredity, which are essentially phenomena manifested by whole organisms—unicellular or multicellular. The connecting link between one generation and the next is in general the cell. Now the cell is unique in that it can be either a whole organism or a constituent of a higher organism —a peculiarity not shared by any sub-cellular unit. Hence

the lowest common measure of development and heredity, the lowest unity in terms of whose modes of action the problems may be rationally stated at all is the cell-organism. Sub-cellular units such as chromosomes or chromomeres may have their importance as conditioning development and heredity within organismal unities, and there may even be direct transmission of special substances from cell to cell, but it is fundamentally wrong in method to ascribe either to such substances or to such sub-cellular units (and *à fortiori* to abstract and hypothetical units like genes or biophors) the essential determination of the phenomena of development and heredity, or to attempt to explain these phenomena of organisms in terms of sub-organismal units. The modes of action of the organism can be developed and displayed only by the organism as a whole, and they can be transmitted only by the new organism which it makes, usually though not invariably in the form of a single cell, carrying *in potentia* the modes of action of its progenitor. The true germ-plasm must be the cell-organism.

These considerations in themselves are sufficient to eliminate all theories which attempt to explain development and heredity in terms of a specific germinal substance, of a 'material basis of heredity', contained within the cell, for these are palpably inadequate to express or explain the facts. The germ-plasm or material basis is a conceptual fiction imposed upon the facts by the exigencies of the mechanistic method. If the germ-plasm disappears there disappear also all representative particles, determinants and genes. All that these concepts were invented to explain can be equally well accounted for by the conditioning action of intra-cellular units such as the chromosomes (see Chapter XIV, pp. 285–7). The purely physico-chemical theories of development also are seen from the organismal point of view to be unequal to the task they attempt, for the simple reason that development cannot possibly be explained in terms of substance, or of physico-chemical system, but only in terms of individual organic unities and their activities.

In considering the phenomena of hereditary transmission

from the organismal point of view it will be necessary to analyse carefully the respective parts played by the organism, the cell, the intra-cellular units, and any specific substances that may be involved, for it is already clear that transmission may mean different things when applied to these different objects; there may be a direct physical sharing out of specific substances from cell to cell, or a handing on of specific metabolic processes associated with intra-cellular units such as the chromosomes, or the inheritance of the general developmental potentialities by the cell-organism which we call the fertilized egg. How this last process is to be conceived is indeed one of the deepest and most inscrutable problems that confront the human intellect, and it is far from being solved. This much is however abundantly clear, that the inheritance of the modes of action of the organism as a whole and of its constituent, collaborating parts, must be on a different level altogether from the mere physical transmission of substances or even of the metabolic rhythms of sub-cellular units. We shall see that the problem of transmission is closely linked up with the general problem of reproduction (see pp. 302–4 below).

With regard to differentiation and to the course of development as a whole, these can no longer be thought of as due to the mysterious determinant action of a hypothetical germinal configuration or of any intra-cellular mechanism whatsoever. Weismann's attempt to explain development as due to the orderly disintegration of a determinant-complex must be regarded as faulty in conception and useless in practice. We must take the facts as they are, and not invent complexities to account for the baffling simplicity of the process. The future task of organismal biology will be to analyse the facts of development—differentiation, harmony, autonomy, regulation—in terms of the modes of action of the organism as a whole, both as conditioned, and as executed, by the activities of the parts. It will pay much attention to the fundamental fact of differentiation and limitation of function.

It were premature to attempt here to enumerate all the fundamental activities or modes of action of the whole

organism, whether unicellular or multicellular, but the more important may be briefly mentioned. There is first of all the group of metabolic functions—assimilation, dissimilation, excretion, respiration, and the like—those that Bichat called the functions of the vegetative life. Closely connected with these are the functions which have to do with the production, maintenance, and restoration of form, both the form of the single cell and the arrangement of differentiated cells to constitute organs and organisms. These may be called the morphogenetic or morphoplastic functions, and are of special importance in the study of development. A third great group comprises those associated with the behaviour of the organism in relation to its external environment and to its own body; they include on the one hand sensory perception in its different forms—extero-, intero-, and proprioreception—and on the other hand responses of various kinds. Other fundamental capabilities of living things, which apply to or affect the more special functions, are the power of mnemic retention and repetition, and the power of self-regulation so much stressed by Roux.[1]

With regard to the problems of heredity and recapitulation, and generally of the historical basis of development, our new principles render possible a line of attack which is closed to the mechanist, but was followed with much success by Samuel Butler. We have seen that the modes of action of the organism as a whole must be construed in relation to the past history both of the individual and of its line of progenitors, and this enables us to envisage the possibility of giving some rational account of the stereotyped repetition of developmental rhythm which shows itself as heredity in the broad sense of the word, and of the reminiscence of ancestral states which we signalize in the law of recapitulation. The mechanist can take no account of this historical aspect of development. The further principle that developmental events have objective reference to a future end enables us to

[1] It will be noted that our fundamental organic 'modes of action' correspond roughly with Roux's 'complex components', which were, however, attributes of cells.

interpret the phenomena of non-functional differentiation and generally all cases of anticipatory action—or at least indicates the line along which such explanation is to be sought. It will probably be found that there is a close relation between past experience and anticipatory action, so that the one may explain the other, through some law of organic habit as yet undiscovered. Looked at from this point of view, the much-debated question of the transmission of acquired characters or of acquired experience takes on a new aspect.

In conclusion, and as a preliminary to the fuller discussion of the question which will be undertaken in the remaining chapters, let us consider very briefly the significance of the cell in relation to the organism as a whole and to reproduction. The question is of great importance methodologically, in connexion with the principles of organismal biology, and for this reason it will be dealt with in some detail in the present book. It is a test case for our thesis that the whole is more than the sum of its parts.

We have seen that in two respects the cell is a specially important unit; first, because it is the lowest unit that is capable of independent life, the simplest type in which the phenomena of life can be fully manifested, and second, because in multicellular organisms reproduction is as a rule carried out through the agency of single cells, which represent *in potentia* the whole organism. The egg-cell is therefore a true 'cell-organism'. One must remember that the fundamental unity with which we deal is the organism, and that it is only when the cell is at the same time an organism that it acquires a particular significance. As a constituent or part of a multicellular organism it has much less importance. According to our principles, we cannot resolve the activities of the whole multicellular organism into the activities of its component cells. As De Bary pointed out long ago, it is the organism that makes the cells, not the cells that make the organism. We shall see in the next chapter that from the point of view of the organism as a whole the cell is mainly a 'metabolic convenience', that the association of nuclear and cytoplasmic substance in the size-

relations characteristic of cells is primarily conditioned by the nature of metabolic processes, and by the relation between the surface and volume of the nucleus.[1] As a necessary condition for metabolism, and therefore for life, the cell-type of organization must characterize living things, and it is only when the scale of magnitude required is small that the cell acquires the rank of organism. As a constituent of a multicellular body it has much lower rank and significance. We shall see that the cell-theory has much exaggerated the importance of the cell, and obscured the importance of the organism. In considering the relation of the cell to differentiation we shall see that the egg-cell is essentially not merely a cell, but the organism-to-be, and that segmentation and nuclear division have little to do with differentiation. In the succeeding chapters we shall develop this question of the relations between the organism and its parts (cells, nuclei, chromosomes), and consider the bearing of our conclusions on the general theory of development, heredity, and reproduction.

[1] This view of the cell is briefly outlined in J. G. Adami, *The Principles of Pathology*, vol. i, London, 1908, pp. 37–8. It is implicit in Sachs's 'energid' theory.

XI

THE PHYSIOLOGICAL INTERPRETATION OF THE CELL-THEORY

THE cell-theory in its earliest form, as shaped by Schwann and Schleiden, was essentially physiological. Cells were regarded as centres of metabolic activity, and the organism as a colony or state built up of these semi-independent units. The morphology of the cell was at that time not well understood: Schwann thought that nuclei arose by a sort of crystallization or condensation; and the fundamental fact that nuclei are formed only by division from a pre-existing nucleus was not fully established until some years later. Gradually, however, as interest in the new science of cytology spread, the morphological aspect became more prominent, and the standard definition of the cell as a mass of protoplasm containing a nucleus, proposed by Max Schultze in 1861, was couched in terms of structure only. As a general definition this holds the field even at the present day.

Clearly it is a wide and formal definition: it covers for instance such diverse things as a tissue cell, a Protozoon, and a fertilized ovum. These have all a common structural characteristic—the presence of a nucleus surrounded by cytoplasm—and may therefore properly be classified as cells. It does not follow, however, that each is sufficiently defined by being called a cell; we shall find reason later to maintain that a tissue cell cannot be adequately characterized without reference to the organism of which it forms an integral part, and that both the Protozoon and the ovum are better defined as organisms than as cells. There is a logical trap for the unwary in any simple and abstract classification which relates to only one characteristic common to a series of objects. Because certain objects can be classified as cells in respect of a common structural quality, it does not follow that they are in other respects homologous, nor that they are fully and adequately characterized by the description 'cell'. This is a

fallacy into which it is easy to slip unconsciously, and it has played its part in the elaboration of the cell-theory in its more extreme forms.

The simple definition of the cell to which we have alluded calls attention to a fundamental peculiarity of all organisms, namely the intimate association of formed nuclear and cytoplasmic substance. No living thing is at present certainly known in which this dualism of substance is not found. As a rule, one or more definite nuclei occur, but bacteria, blue-green algae, and some other forms have, instead of a nucleus, scattered granules of nuclear matter (chromidia). In this chapter we shall consider the physiological significance of this dualism of substance, and particularly the size-relations which characterize it, attempting thus to get back to a physiological interpretation of the cell-theory. Having done this, we shall in subsequent chapters consider in more detail the status of the tissue-cell, the Protozoon, and the ovum in relation to the cell-theory, and finally we shall attempt to correct the over-emphasis laid on cellular activity in development, and restate the early processes of development in terms of the activity of the organism as a whole.

2. Apart from the forms with chromidial nuclei, which have solved the problem of achieving an intimate association of nuclear and cytoplasmic matter by the simple device of dispersing the nuclear substance throughout the cytoplasm, all organisms display a *nucleate* structure. Not all however show a *cellular* structure, that is, a division into more or less separate units each consisting of 'a mass of cytoplasm containing a nucleus'. Some Protozoa are bi- or multi-nucleate, as are also some tissue cells, and there is the very striking and significant case of the *Siphoneae* among the Algae. Forms such as *Caulerpa* and *Acetabularia* reach a very considerable size (several inches in length), and show much external differentiation of structure—'leaves', axis and rhizoids in *Caulerpa*—while showing no internal differentiation into separate cells. There is but one cell-wall and one cell-cavity, traversed it may be by trabecular supports, but there are numerous small nuclei scattered through the cytoplasm,

being specially abundant at the growing points. Are these forms to be regarded as multicellular plants or as multinucleate unicellular plants? If they are to be ranked as unicellular, then the simple definition of the cell must be considerably enlarged to include them. If on the other hand we keep to the definition of the cell as a nucleus with its associated zone of cytoplasm, then the *Siphoneae* are multicellular plants without internal cell-walls.

The confusion arises chiefly from the associations of the word 'cell'. This in its general, non-technical meaning signifies a volume enclosed by a definite wall, and it was the right word to adopt as a technical term in the early days, when the cell-wall was thought to be an essential part of the definition of the cell. The great majority of plants, particularly, show a cellular structure in this proper sense of the word. But the word is clearly ill-adapted, on account of its general implications, to describe the state of affairs in Metazoa generally, and particularly in multinucleate 'cells', syncytia and 'non-cellular' algae and fungi.

To get rid of this source of confusion, J. von Sachs proposed[1] to limit the word cell to such units as are clearly demarcated by a cell-wall or cell-membrane, and to introduce the word *energid* for the more general concept of a nucleus with its associated cytoplasmic field of influence. A multi-nucleate Protozoon would, from this point of view, be regarded as a cell containing a number of energids; so also a siphoneate alga would be a cell inhabited by numerous energids. It is worth while to give Sachs's own definition of the term: 'By an energid I mean a single nucleus together with the protoplasm controlled by it, and I conceive it in such a way that a nucleus with its surrounding protoplasm is to be thought of as a whole, and this whole as an organic unity both in a morphological and in a physiological sense' (p. 1150). In Sachs's view energids are the real constitutive units both of plants and of animals—cellular structure is something superadded. The facts show, he says, that to a certain minimum amount of protoplasm there belongs a nucleus, and

[1] 'Energiden und Zellen', *Gesam. Abhandl.* ii, Leipzig, 1893, pp. 1150–5.

that when this quantity of protoplasm increases, further nuclei become necessary to maintain its energy (p. 1151). The word was chosen to emphasize the *energy* aspect of the nucleus-cytoplasm relation, and it is clear that Sachs considered the energid to be essentially a physiological or metabolic unit. It may of course also be a structural unit, but morphological separateness is no part of its definition. The cell on the other hand *is* a morphological concept, according to Sachs's definition of it as a unit enclosed by a cell-wall or cell-membrane.

We shall consider Sachs's general views on the cell-theory in more detail later (pp. 212–3, 217–8), but for our present purpose his conception of the energid as a physiological unit is the important thing. Our thesis in this chapter is precisely that the cell, or better the energid, is fundamentally a metabolic unit, and it is *as such* that it underlies all organic structure, and all the special activities of the organism, including development.

Using Sachs's nomenclature, we can say that, with the exception of the forms possessing a chromidial nucleus, all organisms are composed of one or more energids, though not all organisms are built up of cells. Or we can use our earlier expression that all organisms show a *nucleate*, but not all a *cellular* structure. We lay stress accordingly on the nucleus with its associated plasma rather than on the 'cell'. The formation of separate cellular units, important and widespread though it is (see below, pp. 217–9), remains a secondary phenomenon.

3. What is the nature of the physiological relationship between nucleus and cytoplasm, which necessitates their intimate spatial association? The general answer to this question was given by Schwann himself, who considered that cells were the essential agents in nutrition and growth: 'The ground of nutrition and growth', he wrote, 'lies not in the organism as a whole, but in the separate elementary parts, the cells.'[1] The anatomist Goodsir, in 1845, likewise spoke

[1] *Mikroskopische Untersuchungen*, 1839, p. 228. The point is fully discussed in my *Form and Function*, 1916, pp. 182–5.

of cells as centres of growth and nutrition.[1] Coming to more modern days, we note that Rauber, in a paper of very great importance for the cell-theory,[2] took the similar view that the function of the nucleus was essentially a trophic one. He remarked upon the great uniformity of the nucleus throughout the most diverse modifications of the cytoplasm:

'The structure of the nucleus is diversified (*vielgestaltig*) only during the periods of division. In the resting stage its structure, even with respect to the most diverse tissues of the adult body, is a monotonous one. The same thing holds good with its chemical composition. In this respect the nucleus stands in complete contrast to the multiform protoplasm. The function of the nucleus can only be one which is independent of the metamorphoses of the protoplasm, a function which the most diverse protoplasmic structures all equally demand. It can only be a trophic function' (p. 251).

Sachs considered his energid to be 'essentially a primary energy-element of the organism, and for that reason the primary element in the processes of form-production (*Gestaltungsvorgänge*)'.[3] He discusses the relation of nucleus and cytoplasm more fully in a paper of 1895,[4] and concludes that the nucleus is the seat not so much of chemical as of morphogenetic energy (*Gestaltungsenergie*). He considers that the function of the cytoplasm is primarily 'kinetic', having to do with the reception of stimuli and with response by movement or by change of form. The fact that the nuclei are crowded together at the growing points, both in cellular and in non-cellular plants, and in cellular plants are at such points very large in proportion to the size of the cells, points also to the conclusion that the nucleus has to do mainly with constructive metabolism and growth.

The same conclusion emerges from Haberlandt's[5] observations on the position of the nucleus in plant cells in relation

[1] See D'Arcy W. Thompson, *On Growth and Form*, 1917, p. 157.

[2] A. Rauber, 'Neue Grundlegungen zur Kenntnis der Zelle', *Morph. Jahrb.*, viii, 1883, pp. 233–338.

[3] Ibid., p. 1155.

[4] 'Physiologische Notizen, ix, Weitere Betrachtungen über Energiden und Zellen', *Flora*, lxxxi, 1895, pp. 405–34.

[5] G. Haberlandt, *Ueber die Beziehungen zwischen Funktion und Lage des Zellkerns*, Jena, 1887.

to the processes of growth, and particularly to the formation of the cell-wall. The nucleus lies near the point of most active growth, and is closely applied to such parts of the cell-wall as are undergoing thickening or extension. A similar study by Korschelt,[1] with reference particularly to ovarian eggs and secreting cells in Insects, also demonstrates the great part played by the nucleus in the metabolic processes of the cell. He found that in the ovarian egg the nucleus is concerned with taking up nutritive substances from the surrounding cells, stretching out processes towards the source of nourishment, increasing thus its active absorbent surface. In the same way the nucleus is concerned in secretion; and in actively secreting cells, e.g. in the silk-glands of Insects, it may greatly increase its surface by branching. In general, the nucleus is to be found in that part of the cell where active absorption or secretion is taking place.

The most direct evidence as to the metabolic function of the nucleus has of course been derived from the numerous experiments which have been carried out with enucleated Protozoa and plant cells.[2] From these the fact emerges clearly that, while enucleate fragments may live for several days, exhibiting characteristic movements, carrying out the physiological functions of respiration and excretion (and even in some cases digestion), assimilation and growth are completely absent, and regeneration is limited to a mere healing of the wound. We may conclude then, with Wilson, 'that destructive processes and the liberation of energy, as manifested by co-ordinated forms of protoplasmic movement, may go on for some time undisturbed in a mass of cytoplasm deprived of a nucleus. On the other hand, the building up of new chemical or morphological products by the cytoplasm is only initiated in the presence of a nucleus, and soon ceases in its absence. The nucleus must, therefore, play an essential part both in the operations of synthetic metabolism

[1] E. Korschelt, 'Beiträge zur Morphologie und Physiologie des Zellkerns', *Zool. Jahrb. (Anat.)*, iv, 1891, pp. 1–154.

[2] For a general account of these experiments see M. Verworn, *General Physiology*, Eng. Trans., 1899, pp. 508–23; Wilson, 1925, pp. 657–62, and B. Sokoloff, 'Das Regenerationsproblem bei Protozoen', *Arch. Protistenkunde*, xlvii, 1924, pp. 143–252.

or chemical synthesis and in the *morphological determination of these operations*' (1925, p. 660).

One must of course bear in mind that there is something abstract and artificial in thus separating and distinguishing the functions of the nucleus from those of the cytoplasm. The nucleus cannot carry out its functions save in association with the cytoplasm, and the cytoplasm deprived of its nucleus soon 'runs down' and dies. As Verworn points out, 'between the protoplasm and the nucleus a mutual exchange of substance takes place, without which neither of the two parts of the cell can continue to exist. In other words, both nucleus and protoplasm take part in the metabolism of the whole cell and are indispensable to its continuance' (1899, p. 518). The elementary unit is the cell or energid *as a whole*. It is we who separate nucleus from cytoplasm by analytical abstraction—in actual fact their characteristic activities depend upon the maintenance of their intimate relations and interactions with each other. We must therefore correct the abstractness of our analysis by keeping in mind constantly the synthetic unity of the energid as a whole.

Even from the chemical or dynamical standpoint, the energid must be regarded as a unitary system, and its structural differentiation into nucleus and cytoplasm as conditioned by and conditioning the nature of its activity as a whole. This point is put very well by D'Arcy Thompson,[1] in the following passage, which is worth quoting in full:

'From the moment that we enter on a dynamical conception of the cell, we perceive that the old debates were in vain as to what visible portions of the cell were active or passive, living or not living. For the manifestations of force can only be due to the *interaction* of the various parts, to the transference of energy from one to another. Certain properties may be manifested, certain functions may be carried on, by the protoplasm apart from the nucleus; but the interaction of the two is necessary, that other and more important properties or functions may be manifested. We know, for instance, that portions of an Infusorian are incapable of regenerating lost parts in the absence of a nucleus, while nucleated pieces soon regain the specific

[1] 1917, pp. 197–8.

form of the organism; and we are told that reproduction by fission cannot be *initiated*, though apparently all its later steps can be carried on, independently of nuclear action. Nor, as Verworn pointed out, can the nucleus possibly be regarded as the "sole vehicle of inheritance", since only in the conjunction of cell and nucleus do we find the essentials of cell-life. 'Kern und Protoplasma sind nur *vereint* lebensfähig", as Nussbaum said.'

According to Hopkins,[1]

'the cell, in the modern phraseology of physical chemistry, is a system of coexisting phases of different constitutions. . . . On ultimate analysis we can scarcely speak at all of living matter in the cell; at any rate, we cannot, without gross misuse of terms, speak of the cell life as being associated with any one particular type of molecule. Its life is the expression of a particular dynamic equilibrium which obtains in a polyphasic system. Certain of the phases may be separated, mechanically or otherwise, as when we squeeze out the cell juices, and find that chemical processes still go on in them; but "life", as we instinctively define it, is a property of the cell as a whole, because it depends upon the organization of processes, upon the equilibrium displayed by the totality of the coexisting phases' (p. 220).

Having established the fact that the energid is the primary unit in constructive metabolism, we must now go on to consider the significance of the characteristic size-relations of nuclei and their associated cytoplasm.

4. D'Arcy Thompson in that admirable book *On Growth and Form* has called attention to the importance of size or scale in organic structures, with reference particularly to the changing relation between volume and surface in structures of similar shape as their dimensions alter. Surface varies as the square, volume as the cube, of corresponding linear dimensions; hence a small sphere, for instance, has a relatively greater surface in proportion to its volume than a larger sphere.

That nuclei are all of very restricted dimensions is therefore a fact of much significance, and suggests at once that a high ratio of surface to volume is important for the physiological activity of the nucleus.

[1] F. G. Hopkins, 'The Dynamic Side of Biochemistry', Pres. Address to Physiology Section of the British Association, 1913. *Nature*, vol. xcii, pp. 213–23.

The nucleus, in the absurdly named resting stage, when it is in fact most fully active, is bounded by a definite membrane or cortical layer, and all its interactions with the cytoplasm are mediated by this surface of separation. It tends as a rule, unless deformed by the shape of the cell, to assume a spherical or oval form. This shape is by no means ideal from the point of view of exposing a maximum surface, for the sphere is of all bodies that which has the minimum surface per unit volume, but it is probably imposed on the nucleus by physical conditions—surface tension and the like.[1] And of course many exceptions occur—nuclei, as we have seen, may be branched or lobed in special cases, where extra surface is required.

'Nuclei of irregular or amoeboid form are frequent in cells characterized by very active metabolism, in which case the nuclei are often not only of large size but show a marked further increase of surface by the formation of lobes, sacculations, or even, in extreme cases, of complex branches ramifying through the cell. An extreme example of this is offered by the spinning glands of certain insect larvae (Lepidoptera, Trichoptera) in which the nucleus, originally spheroidal, finally assumes a labyrinthine appearance with convolutions occupying a large area in the cell. In other cases the nucleus shows deep infoldings or incisions and sometimes even tubular ingrowths of membrane forming intra-nuclear canaliculi; and it has been shown that such infoldings may unfold or evaginate, thus increasing the nuclear size. In certain types of cells the surface of the nucleus may also be increased by its breaking up into more or less separate vesicles or karyomerites, thus forming "polymorphic" nuclei or nuclear nests.'[2]

It is of course impossible to give a mean size for all kinds of nuclei; the available data are restricted in quantity, and even if they were sufficient to be representative, the mean calculated from them would be merely a mathematical abstraction; further, the size of the nucleus may vary in the individual cell according to its functional activity,[3] and again, there is in general a regular increase in nuclear size from one

[1] D'Arcy Thompson, *On Growth and Form*, p. 165.

[2] Wilson, 1925, pp. 78–9.

[3] See for instance C. F. Hodge, 'A microscopical Study of Changes due to functional activity in Nerve Cells', *Journ. Morph.* vii, 1892, pp. 95–168.

mitosis to the next, when nuclear size is again reduced—a nuclear diastole and systole, as the process was called by Ryder.[1] All that we can do is to quote a few examples of nuclear sizes in diverse groups of organisms and in diverse kinds of cell.

The nucleus of the animal ovum is as a rule relatively large, and there is a steady diminution in the size of the individual nuclei as segmentation proceeds. This may be exemplified by the sea-urchin *Strongylocentrotus lividus*, where the size-relations of nuclei and cytoplasm during early development have been carefully studied by Rh. Erdmann.[2] The eggs were reared under different conditions of temperature, namely at 10° C., 15°–16° C., and 20° C. It is sufficient for our purpose to consider only the first set. The following data are extracted from the table on p. 88:

Stage of development.	*Radius of Nucleus.*	*Volume of Nucleus.*	*Volume of Cell.*
	μ	μ^3	μ^3
2-cells	13·88	10,037	106,250
4 "	7·264	1,605·8	51,063
8 "	6·362	1,081·0	26,290
16 "	5·844	837·8	9,973
32 "	5·76	803·6	6,023
64–132 "	5·41	529·7	2,685·5
Blastula I	4·791	460·5	1,343
Blastula II	4·297	332·4	549·7
Gastrula I	2·97	117·39	292·5
Gastrula II	2·466	62·87	180·7
Pluteus	1·9	28·73	118

The size of the nucleus decreases in steady progression as segmentation and development proceed. So also does the size of the segmentation spheres or cells. For the greater part of the time, the cell-volume decreases at a greater rate than the nuclear volume, the ratio, cell-volume: nuclear volume, falling from 31·8 at the 4-celled stage to 1·6 at the second blastula stage, increasing thereafter to 4·2 in the pluteus.

[1] See E. G. Conklin, 'Cellular Differentiation', in Cowdry, *General Cytology*, Chicago, 1924, p. 550.

[2] 'Experimentelle Untersuchung der Massenverhältnisse von Plasma, Kern und Chromosomen in dem sich entwickelnden Seeigelei', *Arch. f. Zellforschung*, ii, 1909, pp. 76–136.

If we consider the developing egg as a whole, we find that its total volume hardly increases at all until the second blastula stage is reached. This is shown by the following calculation:

Total volume at	2-cell stage—	$106,250 \times 2$	$= 212,500\mu^3$
,, ,,	32-cell ,,	$6,023 \times 32$	$= 192,736\mu^3$
,, ,,	Bl. I ,,	$1,343 \times 170$[1]	$= 228,310\mu^3$
,, ,,	Bl. II ,,	$549{\cdot}7 \times 680$[1]	$= 373,796\mu^3$

The total nuclear volume, however, increases at these stages as follows: 20,074, 25,715, 78,285, and 226,032μ^3. Thus up to the first blastula stage, while the total volume of the cells of the developing egg remains nearly constant, the nuclear substance has increased nearly 4 times. If now we calculate the total surface area of the nuclei (on the assumption that they are spherical) we find the increase to be from 4,339μ^2 at the 2-cell stage to 49,020μ^2 at the first blastula stage, an increase of about 11 times. The result of segmentation and cell-division is then a considerable increase in the amount of nuclear substance relative to cytoplasmic substance, and a much greater increase in total nuclear surface. Even if there were no increase in total nuclear volume during the process, it may easily be calculated that the total nuclear surface would increase considerably—from 4,339μ^2 at the 2-cell stage to 19,788μ^2 at the first blastula stage ($r = 3{\cdot}0434$). The course of events then in the early development of *Strongylocentrotus* affords a good object-lesson in the importance of absolute size in relation to surface area; the 170 small nuclei of the blastula expose collectively 11 times as much surface area as the 2 nuclei of the 2-cell stage, and, presumably, are physiologically more efficient in somewhat the same ratio.

The same phenomenon of increase in total nuclear surface during segmentation is shown clearly in the mollusc *Crepidula*. Conklin,[2] who has studied this form minutely, writes:

'During cleavage the increase in nuclear surfaces is much greater than the increase in nuclear volumes. While the increase in maximum[3]

[1] Erdmann, p. 97.

[2] E. G. Conklin, 'Cell Size and Nuclear Size', *Journ. Exper. Zool.* xii, 1912, pp. 1–98.

[3] Nucleus measured at its maximum volume, i.e. just before division.

nuclear volumes up to the 32-cell stage of Crepidula is about 5 per cent. for each division, the growth in the maximum nuclear surfaces during this period is about 11 per cent. for each division. From the 2-cell to the 70-cell stage the nuclear volume increases only 2·24 times, while the nuclear surfaces increase 5·30 times. In Styela the nuclear volume increases from the 2-cell stage to the 256-cell stage only 4·52 times, the nuclear surfaces increase 13·75 times. Unquestionably this greater growth of nuclear surfaces as compared with nuclear volumes facilitates the interchange between nucleus and protoplasm' (p. 61).

The nucleus or germinal vesicle of the immature egg is in many animals relatively large and relatively inactive; after fertilization and during segmentation the metabolic activity of the egg increases: this is no doubt facilitated by the division of the nucleus into smaller units, which, distributed through the developing egg, expose a larger action-surface than the undivided nucleus.

Possibly also, as Conklin suggests, there is a specially intimate exchange, particularly of substance, between nucleus and cytoplasm at the time of mitosis, when large quantities of material absorbed by the nucleus during inter-mitotic growth are released again into the cytoplasm.

It is interesting to note that Sachs, in his paper of 1895 already referred to, suggests that surface action plays a great role in the physiological activities of the component parts of the energid, and that it is for this reason that these parts are of such restricted dimensions. 'The minuteness of the parts', he writes, 'which react upon one another, inside the energid, both mechanically and kinetically, shows that so-called surface forces are here primarily concerned—forces that can act only at very short distances, but whose effect increases with increase of surface for a given volume' (p. 425). In a previous paper (1893) he had pointed out that in segmentation the splitting up of the zygote nucleus into numerous smaller ones was accompanied by an increase in the activity of the nucleus, the undivided nucleus being physiologically inert, and the developmental processes progressing the more energetically the further nuclear division proceeds. He

drew the tentative conclusion, as we have done, that the rationale of nuclear division in segmentation is to be found in the increase of metabolic activity brought about by increase of total surface.

Reverting to Conklin's paper, we may note some typical dimensions of nuclei in *Crepidula*, for comparison with the data for *Strongylocentrotus*. *Crepidula* differs from the sea-urchin particularly in the fact that the total volume of the cytoplasm increases considerably at the expense of the yolk, which is here abundant, and for a time at a greater rate than the total nuclear volume (p. 33). The mean diameter of the nucleus at the 2-cell stage is 18μ, at the 4-cell stage 16μ, at the 8-cell stage 15μ for the macromeres and 12μ for the micromeres. At the 70-cell stage the nuclear diameter varies from 5μ to 16μ according to the size and type of the cells. In sexually mature individuals the nuclei are smaller—about 4–8μ in epithelial and secreting cells, up to 12μ in large ganglion cells. In *Fulgur*, which has large eggs, the diameter of the nucleus in early cleavage stages is much greater—up to 96μ in cells 4A–4D, before the seventh cleavage.

In the ascidian *Styela* (*Cynthia*), the average diameters of the nuclei are as follows (p. 43):

Before first maturation	54μ
" " cleavage	12μ (♂ and ♀ pronuclei)
2-cell stage	16μ
4 "	14μ
8 "	13μ
16 "	11μ
32 "	10μ
64 "	8μ
128 "	6·5μ
256 "	5·25μ.

With regard to nuclear size in Vertebrates, many data are given by Hartmann[1] relating to the common toad and other Amphibia, and these are summarized in convenient form in

[1] O. Hartmann, 'Ueber den Einfluss der Temperatur auf Grösse und Beschaffenheit von Zelle und Kern, *Arch. f. Ent.-Mech.*, xliv, 1918, pp. 114–95.

Tabulae biologicae.[1] From these tables I have calculated the following means, relating to 66 determinations of nuclear size in many different kinds of tissue at diverse stages of development in *Bufo vulgaris*:

Mean of length $11{\cdot}3\mu$
" breadth $8{\cdot}55\mu$
" surface $93{\cdot}48\mu^2$.

These averages have only a mathematical significance, but they give an approximate idea of the general size of nuclei in this species. The nuclei of the erythrocytes in old tadpoles of *Bufo* measure $8{\cdot}6\times5{\cdot}5\mu$; in adult *Bombinator igneus* the erythrocyte nuclei measure $12{\cdot}9\times7{\cdot}0\mu$, and in *Triton alpestris* $18{\cdot}0\times9{\cdot}6\mu$.

For the sake of comparison, a few data relating to plants may be quoted. Strasburger[2] made measurements of cell-size and nuclear size in the growing points of 40 species of vascular cryptograms and phanerogams. He found considerable variations, mean nuclear diameter ranging from 3μ to 16μ, while cell-diameter varied from 5μ to 24μ. He concluded that in these young cells, before growth and vacuolization took place, the ratio of nuclear size to cell-size was about 2 : 3 (p. 117).

From the few examples given above as to size of nuclei in diverse groups of animals and plants, it is evident that, while there is great variation according to species, kind of cell, and stage of development, the nucleus is always a structure of very restricted dimensions, with a diameter measurable in hundredths or thousandths of a millimetre. It appears reasonable to suppose that this limitation of size is connected with the need for keeping surface large in relation to volume, in order that the nuclear contents may all enter into close and intimate metabolic relations with the cytoplasm. Cell-division, in animals at least, is always initiated by nuclear division, and it may be surmised that the rationale of nuclear division is to keep the nucleus small, in order that its volume

[1] *Tabulae biologicae*, ed. by W. Junk, vol. iv, Berlin, 1927, pp. 328–30.

[2] E. Strasburger, 'Ueber die Wirkungssphäre der Kern und die Zellgrösse', *Histologische Beiträge*, vol. v, Jena, 1893, pp. 97–124.

may not increase unduly in proportion to its surface, and so hinder and slow down its metabolic interchange with the cytoplasm.

We come now to the second point connected with size-relations, namely the size of the cell or energid itself. This is a point which has been very thoroughly discussed in the literature,[1] and for this reason we need not go into it in any great detail. Certain general facts seem to be established. There is a rough correlation between the size of the cell, especially the active cytoplasmic part of it, and the size of the nucleus (karyoplasmic ratio of R. Hertwig), but there are numerous exceptions to the rule. The size of cells appears to be a specific constant, so that large individuals of a species differ from small individuals in respect of the total number of cells, but not in respect of the size of the cells—provided that their chromosome numbers are the same, for a doubling of the number of chromosomes may bring about an increase both in cell-size and in body-size. There is enormous variation in the size of cells—from a bacillus which is barely visible under the highest powers of the microscope to the relatively huge eggs of some birds and sharks. The length of the axon fibre of a neurone may be several feet. It cannot be said then that there is anything like the same restriction on cell-size that there is on nuclear size; we note only that there must be physical continuity between all parts of the cell and its nucleus—cytoplasmic substance cannot exist for any length of time in physiological isolation from a nucleus.

Nevertheless, apart from special cases such as we have mentioned, cells are as a rule quite small objects, measurable in tenths or in hundredths of a millimetre.

For plant cells Sachs gives the mean linear dimension as about 20μ, and points out that whatever the size of the plant may be the size of its cells is to be reckoned in small fractions of a millimetre, and its volume in cubic μ (1895, p. 423). The reason why energids are small is that the sphere of influence of a nucleus is a limited one. Physiologically regarded, the cell, or rather the energid, is the zone of influence of a

[1] See for instance Wilson, 1925, pp. 97–101.

nucleus, which is itself minute; the size of the energid is therefore limited by the distance to which the influence of the nucleus can be transmitted, or by the volume of cytoplasmic substance with which the nucleus can effectively keep in metabolic relations.

Loeb adopts this same physiological interpretation of the cell-theory in a short paper dealing with the function of the nucleus in regeneration.[1] He points out that organic synthesis cannot go on without oxygen and adduces evidence that the nucleus is an oxidation centre. The reason why cells are small is that the cell-substance must remain within effective reach of the oxidative nucleus, otherwise it will perish through lack of oxygen. The cellular or energid structure of living things is then primarily an expression of the fact that cytoplasm must keep within a certain small distance of a nucleus.

Similar views are expressed by Watasé,[2] on general grounds:

'The division of an organism into distinct cell-entities in a multicellular organism is a phenomenon widely distributed, it is true, but still of secondary significance, due to physiological causes, I believe, emanating from the fundamental difference existing between the chromosome and the cytoplasm, the difference between the two being of such a character that makes their mutual association necessary for the existence of each. The chromosome cannot grow beyond a certain bulk, nor is the cytoplasm capable of unlimited growth, without each meeting with a restraining influence from the other, if one may express it in a metaphorical way. The formation of a nucleated cell is, in other words, a secondary adaptation to keep the nuclear and cytoplasmic material within the reach of reciprocal physiological influence of each' (pp. 102–3).

The same is of course true of the energid—or rather it is primarily true of the energid.

5. We may now sum up our discussion as follows. An intimate association of nuclear and cytoplasmic matter underlies all organization and all vital activities. Without

[1] J. Loeb, 'Warum ist die Regeneration kernloser Protoplasmastücke unmöglich oder erschwert?' *Arch. Ent.-Mech.*, viii, 1899, pp. 689–93.

[2] S. Watasé, 'On the Nature of Cell-Organization', *Wood's Holl Biol. Lectures for 1893*, Boston, 1894, pp. 83–103.

this dualism of substance, constructive metabolism, growth, and development are impossible. It is therefore a primary condition of all continuing life, and of all special manifestations of life—genetic continuity, fertilization, development, growth, regeneration, and so on. Apart from forms in which nuclear matter is dispersed throughout the cell, this dualism of nuclear and cytoplasmic substance appears in the shape of a small formed nucleus with its associated cytoplasm—the energid. An energid type of organization characterizes therefore the vast majority of organic forms. The energids, being primarily concerned with organic synthesis, may be regarded as the metabolic centres of the organism.

From this essentially physiological point of view, the organism must be regarded as a protoplasmic mass containing, for the purposes of metabolism, one or more nuclei, one or more energids. From this point of view, the energids cannot be properly considered as independent or semi-independent units composing the organism, but rather as structures specialized for the metabolic functions of growth and repair, and as such subservient to the needs and activities of the organism as a whole. The true biological unit is therefore not the energid, but the organism, whether this is made up of one energid or of many.

This physiological formulation of the cell-theory is one which is in fact gradually replacing the older ideas about cells.

Doncaster for example[1] states boldly that 'to regard the organism as built up of discrete cells which co-operate physiologically but are fundamentally independent is a false conception' (p. 2), and he contrasts the old with the new view as follows:

'The cell theory in its original and crude form regarded an organism as composed of a horde of discrete units which co-operate for a common purpose and are modified in various ways to make that co-operation effective, much as a human community consists of many separate individuals, having different occupations and co-operating for their common good. According to this idea the individuality of any organism arose from an integration of the in

[1] L. Doncaster, *An Introduction to the Study of Cytology*, Cambridge, 1920.

dividualities of its separate cells, and is thus a corporate individuality such as may exist in a school or a regiment. Nowadays, however, opinion tends in the opposite direction—to regard the organism as the individual, and the cells not as units of which it is built up but rather as parts into which it is divided in order to provide for the necessary division of labour involved in so complex a process as life' (p. 3).

There can be no doubt as to which of these two views of the organism the energid theory leads us to adopt. Physiologically regarded, the organism is one, and its cells or energids are merely organs of the whole.

The energid conception of the organism requires of course a little correction or enlargement. In most multinucleate organisms there is more implied in cell-formation than a mere multiplication of undifferentiated energids, such as takes place in 'non-cellular' plants.

The formation of more or less discrete cells, and their differentiation into different types, clearly plays a great part in the development of any complex multicellular organism. This is a point which we shall consider in more detail in the next chapter. But the energid conception represents the most general point of view that we can take, for it is applicable to all forms without exception that have a formed nucleus, whereas the cellular conception is difficult to apply satisfactorily to Protozoa for instance and 'non-cellular' plants. We are justified therefore in regarding the energid conception as the more fundamental.

We saw in our discussion of the facts that nuclei are all of very restricted dimensions, being measurable in hundredths or thousandths of a millimetre, and that energids also are limited in size, though not so strictly as are nuclei. We suggested also, as a possible or probable physiological explanation, the hypothesis that the surface of the nucleus must be kept large in proportion to its volume, in order that all its constituents may enter into intimate relations with the cytoplasm of the energid. However that may be, there is no doubt about the empirical fact of the minuteness of nuclei, nor of the conclusion reached by Sachs (see above, p. 200) that to a certain minimum amount of protoplasm there belongs a

nucleus, and that when this quantity of protoplasm increases, further nuclei become necessary to maintain its energy. It follows then that the number of nuclei is, in the main, a function of the size of the organism. An organism composed of one energid is necessarily a small organism: a large organism must necessarily contain many energids. Accordingly the main difference between Protozoa and Metazoa, and between unicellular and multicellular plants, is simply one of size. We shall see later that the unicellular organism is strictly comparable not with the single cells of the multicellular organism, but with that organism as a whole.

Another simple deduction from the facts about the energid is that, when for any reason vital phenomena must take place in minimal dimensions, the type of the unit concerned must be mono-energid. Hence, for instance, the mono-energid character of ova and spermatozoa.

XII

THE CELL AND THE ORGANISM

THOSE organisms which, consisting of one or of many energids, show no differentiation into separate cells are as a rule comparatively small in size and simple in structure; large and complex organisms are invariably multicellular. It appears then that a cellular structure is a necessary condition for any great degree of growth and differentiation. The reasons for this are not far to seek.

In plants, the formation of resistent cell-walls is enormously important in imparting rigidity, and so enabling a great elaboration of external form and internal differentiation to take place. The supporting structures of the cellular plant, its exo- and endo-skeleton, are essentially formed by its cell-walls and their derivatives. The separation of protoplasmic cells by means of definite walls, though the cells may be connected by inter-cellular bridges, also permits of a certain segregation and diversity of metabolic processes, which are carried out, as it were, in separate little laboratories. Compared with the Siphoneate algae, which are the largest and most highly developed of non-cellular, polyenergid organisms, cellular plants differ mainly and primarily in this formation of definite cell-walls; the other differences are derivative from this primary one. The point is well put by Sachs,[1] who writes of the *Siphoneae* (which he calls *Coeloblasteae*) as follows:

'. . . in the protoplasm of these plants a certain quantity of nuclear substance (especially the nuclein characteristic of it) is distributed in formed portions and at small intervals, and is especially aggregated in the growing points. From this fact, we obtain once more, as we have already obtained from other sides, a certain insight into the true significance of the cellular structure of plants. We need only imagine in a not too complex cellular plant (a higher Alga, a Moss, or even a vascular plant) that in the substance enveloped by the outer walls of the epidermis, the cell-walls are simply wanting; whereas the proto-

[1] J. von Sachs, *Lectures on the Physiology of Plants* (Eng. Trans.), Oxford, 1887.

plasm, with the cell-nuclei distributed in it, behaves essentially as if these cell-walls were present. Thus we have, on the whole, the structure of a *Coeloblast*. On the contrary, we need only imagine the inner cavity of such a *Coeloblast* to be divided up by numerous transverse and longitudinal partition-walls into very numerous small chambers, each of which encloses one or several of the cell-nuclei present, and we should thus have an ordinary cellular plant. It is however very easily intelligible that not only the solidity, but also the shutting off of various products of metabolism, the conduction of the sap from place to place, and so forth, must attain greater perfection if the whole substance of a plant is divided up by numerous transverse and longitudinal walls into cell-chambers sharply separated off from one another' (p. 109).

Even for plants, however, this does not give the whole story; there are other advantages in a cellular structure besides those mentioned by Sachs. In particular, the matter of surface-area has to be considered. For the life of the energid a supply of oxygen and nutritive substances is essential, and these must be taken up by its surface. It would be impossible, for instance, for energids to exist in a mass of any thickness, for those in the middle would be asphyxiated and starved. For this reason, the energids of a Siphoneate alga form a thin layer, bounded externally by the common wall and internally by the common vacuolar system. In cellular plants, access to nutrient salts is arranged for by a system of water-transport, and to oxygen by a system of intercellular air-spaces, and most cells have their own private *milieu interne* in the form of an intracellular vacuole.

In animals, the general circulating body-fluid, blood or lymph, plays a greater role than in plants, as the source of the means of life, and all animal cells are bathed in greater or lesser degree by this internal medium. In animals, rigid cell-walls are of little importance, and the rationale of cell-formation is to be sought rather in the necessity for exposing at least part of the surface of the energid to the internal medium, and still more in the advantages offered by separate cells for histological differentiation and the building up of elaborate organs.

The advantages of cellular structure in animals were briefly

discussed by Rauber in his paper of 1883.[1] Following Leuckart, he pointed out that by the formation of separate cells the surface area was increased, thus facilitating the metabolic processes of the energids. Chemical and histological differentiation was also furthered, and cells could be arranged and built up into structures of great complexity—they had thus an architectonic value (pp. 333–4). Of more modern writers, O. Hertwig may be mentioned, who discusses the question on much the same lines as Sachs and Rauber.[2] It merits fuller treatment, especially from a biochemical standpoint, than can be accorded to it here. We may however safely draw the conclusion that a cellular structure is physiologically an advance upon a plasmodial or syncytial state, and a necessary pre-condition of any great elaboration of internal organization.

2. While adhering to the view that an energid organization is the most general and fundamental of all, and has its *raison d'être* in metabolic necessities, we must recognize that the majority of organic types are composed of more or less discrete, more or less independent cellular units.

We may now profitably consider, purely on the basis of observed fact, just how far the tissue cells of multicellular organisms are separate and independent morphological units, just how far, that is to say, the cell theory is an accurate description of the intimate structure of these organisms. Are the cells of Metazoa and Metaphyta separate and distinct, so that the organism may be properly regarded as a cell-state or cell-colony, or are they so intimately connected with one another that the multicellular organism must be regarded as a syncytial whole, secondarily differentiated into energids and cells?

Both views are held at the present day, and there is not a little conflict of evidence as to which is observationally correct. Though, as we shall see, the question is not of crucial or decisive importance in relation to the theoretical aspect of the cell-theory, it will not be without interest, in connexion with the

[1] *Morph. Jahrb.* viii, 1883, pp. 233–338.
[2] *Allgemeine Biologie*, 6th and 7th edit., Jena, 1923, pp. 501–2.

general problem of the relation of the cell to the organism, briefly to survey the more important evidence bearing upon the question. We shall find that neither view is wholly correct, but that each contains essential elements of the truth.

3. In general, those who have looked for and found intercellular connexions have been impressed with the continuity of substance throughout the organism and have accepted the view of the organism as syncytial. Thus Heitzmann in 1873 held that even when distinct cell-walls were present they were traversed by strands of protoplasm, by means of which the protoplasts remained in protoplasmic continuity. He conceived the whole body as being a more or less continuous mass, with cells as nodal points in a general network of protoplasm.[1] Intercellular connexions were demonstrated to be widespread in plants by Tangl, Gardiner, Kienitz-Gerloff, A. Meyer and others, and Sachs's view[2] that the cellular plant is essentially a continuum interrupted by perforated cell-walls received much support.

In animals also, intercellular bridges were discovered in many different kinds of tissue, and Adam Sedgwick in particular laid stress upon cellular continuity in the early stages of development. In embryos of *Peripatus capensis* he found that for some time all the cells were connected up by protoplasmic bridges, and in developing Elasmobranchs he described the mesenchyme tissue as being a reticulum of pale non-staining substance containing nuclei at its nodes. Even the endoderm and ectoderm he regarded as being simply specialized parts of the reticulum, in which the meshes are closer and the nuclei more numerous and arranged in layers. In general the nerve-crest and other epithelial tissues were to be thought of as centres of growth and of the multiplication of nuclei.[3]

[1] Wilson, 1925, pp. 103–4.

[2] 'Fundamentally, every plant, however highly organized, is a protoplasmic body coherent in itself, which, clothed without by a cell-wall and traversed internally by innumerable transverse and longitudinal walls, grows; and it appears that the more vigorously this formation of chambers and walls proceeds with the nutrition of the protoplasm, the higher also is the development attained by the total organization' (*Lectures*, p. 84).

[3] A. Sedgwick, 'On the Inadequacy of the Cellular Theory of Development,' *Q.J.M.S.*, xxxvii, 1895, pp. 87–101.

The existence of cell-bridges and connexions in several kinds of tissue—epithelial, connective, and muscular—is generally recognized, and it is also an agreed fact that in the development of many forms, particularly of Arthropods, the earliest stages of 'segmentation' may be syncytial.

Some writers have attempted to establish the general thesis that all the cells of the body are, or have been at some stage, connected with one another, and that accordingly the organism is essentially a plasmodial whole, secondarily differentiated into cells. In particular, Emil Rohde has championed this view in a long series of publications. He has summarized his observations and deductions in a recent comprehensive paper,[1] which we may consider in some detail, as typifying this particular interpretation of the organism and its cells.

He deals at great length, adducing a wealth of illustrative detail, with the ontogenetic and phylogenetic origin of cells, and with the facts of histology and histogenesis, both in animals and in plants.

With regard to the origin of tissues he concludes that all tissues originate and develop from multinucleate plasmodia, and for the most part retain permanently their plasmodial character. The tissue cells are not the direct descendants of the cells of the embryo, but secondary or tertiary formations which originate *de novo* in the primary multinucleate plasmodium. Histological differentiation, that is to say, the formation of fibrils and ground-substances, is not bound up with cells, but takes place in the primary multinucleate plasmodium, usually before the appearance of tissue cells. Tissue cells in many cases make their appearance as a consequence, not a cause of histological differentiation (p. 469). While accepting the proved fact that all nuclei arise from pre-existing nuclei, Rohde rejects the further generalization (which we owe to Virchow) that cells arise only by division of pre-existing cells. *Omnis cellula e cellula* he regards as a definitely incorrect statement of the facts. He considers that

[1] Emil Rohde, 'Der plasmodiale Aufbau des Tier- und Pflanzenkörpers', *Zts. f. wiss. Zool.* cxx, 1923, pp. 325–535.

there is no necessary connexion between nuclear division and cell-division, and he gives as an illustration, among others, the process of cell-formation in the *Siphonocladaceae*, which are a group of Algae standing just above the *Siphoneae* and with them classified as Siphonales. These forms begin their development as multinucleate plasmodia, just like the *Siphoneae*; as development proceeds, cellulose partitions are formed cutting off multinucleate sections of the plasmodium. These partitions increase in number, and the areas separated become reduced in size, till finally cells containing only two nuclei are formed. In the development of the higher fungi a similar progressive septation takes place, which results in the formation of typical uninucleate cells. Some of the higher forms of the *Siphonocladaceae* have a multinucleate apical 'cell', which cuts off from itself basal 'cells', which are likewise multinucleate.

In the development of many animals and plants there is a stage in which nuclear division goes on without formation of cells; these arise later; in some cases, e.g. in the early development of Myriapods, the cells (yolk pyramids) are formed independently of the nuclei, which later move into them (see Rohde's Fig. 16). In general, he regards cells as having arisen by differentiation from a plasmodium, and the same applies to all manner of fibrils and other specialized products of protoplasmic activity, which develop with no particular relation to cell-boundaries, in the ground-substance of the plasmodium. A neurone for example arises by the differentiation of a part of the plasmodium; of the nuclei contained in this portion one increases in size and becomes the large nucleus of the ganglion cell, the others remain small and form the nuclei of the neuroglia cells and the sheath cells, while at the same time the protoplasm round the enlarged nucleus becomes differentiated into neural substance. The ganglion cell is therefore in Rohde's view a new formation, arising by differentiation from a plasmodial beginning and only gradually separating itself off from the adjacent cells which are simultaneously formed as subsidiary to it. In the same way the neurofibrillae, which later form the axon

fibre, are differentiated *in situ* from a syncytial or plasmodial continuum.

It is unnecessary to refer to the great mass of evidence that Rohde has adduced in favour of his view that tissue cells originate, not primarily by cell-division, but by differentiation from a multinucleate continuum; enough has perhaps been said to indicate the kind of evidence brought forward. We note particularly that he regards the energid conception of the organism as the fundamental one, and cells as something secondary. Assimilation, growth, and differentiation can go on perfectly well in the absence of cells, as the Siphoneae clearly demonstrate to us, and cells are formed for physiological reasons, for the purpose of giving support and rigidity to the organism, and ensuring the better nutrition of its parts (pp. 523 and 525).

His general conclusions may be summed up as follows:

'Every animal and plant individual represents a unitary protoplasmic mass, either uninucleate or multinucleate, from which there can separate off uninucleate or multinucleate portions as independent protoplasmic masses (the so-called free cells of the text-books: red and white blood corpuscles, mesenchyme cells, sex-cells, &c.). The multinucleate plasmodium, of which the animal body consists, contains two kinds of living substance: protoplasm and metaplasm. Cells in the ordinary sense are not morphologically equivalent structures, standing at the same level of individuality or organization, but quite heterogeneous and diverse formations, fundamentally different not only in development but in structure and potencies. Plasmodia and cells alternate with one another in the development of animals and plants.

'Metazoa and Metaphyta originate phylogenetically not from a colony of cells, but from multinucleate plasmodia; in the ontogenetic and histogenetic development of cells in Metazoa and Metaphyta there is a repetition of the processes which took place in the phylogenetic origin of cells.

'Cells are not of the fundamental importance in the animal and the plant body which the ruling cell-theory attributes to them, but are secondary phenomena of merely secondary importance' (p. 326).

There is from Rohde's point of view no fundamental difference between 'unicellular' organisms and multicellular. The Protozoon, for example, is not to be regarded as homo-

logous with the tissue cell of a Metazoon, but as the equivalent of the whole body of the latter. In both, 'histological' differentiation takes place essentially in the same way—in one case in a small, usually monoenergid unit, in the other in a larger, polyenergid plasmodium. The cortical layer of the Protozoon is from this point of view strictly comparable with the ectoderm of Metazoa, and arises in essentially the same way, by differentiation out of a protoplasmic continuum (pp. 489–91).

The contrast between Rohde's view of the cell and the organism and the classical cell-theory is sufficiently striking. Instead of the composite, colonial cell-state, made up of semi-independent, collaborating units—essentially an analytical view—we have the organism conceived as a unitary and unified whole, with nuclei scattered throughout its substance, and cells appearing, as physiological needs dictate, in the form of cytoplasmic differentiations, more or less independently of the nuclei, which show a uniform structure and little or no differentiation. Undoubtedly it is easier to think of the organism as a unitary whole on the plasmodial conception than on the cellular.

4. There are however many facts which are not easily reconcilable with the plasmodial conception. In the first place, separate free-living and free-moving cells are found in many animal organisms, and in the second place, in many animal tissues the cells show a considerable measure of functional independence, and the new tissue cells do arise by division of the existing cells. Modern work on tissue culture has also strengthened the conviction that the cells of Metazoa possess to a considerable degree functional and structural independence.

Many writers therefore, while admitting the evidence for protoplasmic connexions between cells, prefer to keep to the cell-theory of the organism, finding in it a powerful weapon of analysis. Thus Wilson writes apropos of the cell-theory: 'Its value as a means of biological analysis needs no other demonstration than the immense advances that it made possible. Inevitably in practice we treat cells as distinct,

though closely co-ordinated, elementary organisms or organic units; and although some writers have questioned the validity of this procedure it nevertheless remains an indispensable means of analysis.[1] (That word 'inevitably' should give us pause—it is generally an indication of an unconscious or unacknowledged *parti pris.*) Wilson accordingly throughout his book proceeds 'upon the assumption, if only as a practical method, that the multicellular organism in general is comparable to an assemblage of Protista which have undergone a high degree of integration and differentiation so as to constitute essentially a cell-state'.[2] It will be of interest to consider in brief outline some of the more striking evidence in favour of the functional and structural independence of the tissue cell.

The development of micro-dissection methods by Barbour, Kite, and Chambers has furnished a new means of studying directly the living cell and its connexions with its neighbours. Chambers[3] draws the general conclusion from his extensive researches by these methods that intercellular bridges, while of common occurrence in plants, are comparatively rare in animals, what has been taken as such being really cement substance.

'In the majority of the cell groups in the metazoan body', he writes, 'there is no evidence whatever for the existence of actual protoplasmic bridges between the individual cells. It is highly probable that protoplasm exists as a morphological and physiological unit in each cell of the body. Some of its functions may be more highly specialized in one group of cells than in another, and the secretions of one group of cells may profoundly affect another; but as regards the fundamental vital phenomena, each cell lives out its own existence' (p. 243).

He points out that all cells, both ectoderm and endoderm, that are in contact with the environment external or internal, are covered on their exposed surfaces by a continuous, structureless membrane; the ciliated epithelium in the mouth of the frog, for example, can be torn off in strips which, if dissociated by means of the micro-dissection needle,

[1] 1925, p. 102. [2] 1925, p. 103.
[3] R. Chambers, 'The Physical Structure of Protoplasm as determined by Micro-dissection and Injection', in Cowdry, *General Cytology*, Chicago, 1924.

are found to be held together mainly by a structureless cuticular border continuous over their originally free surface (p. 254). Tissue culture work has also thrown doubt upon the reality, or the physiological significance, of intercellular connexions. Thus the Lewises[1] conclude that the mesenchyme cells of the vertebrate embryo form not a true syncytium, but an adherent reticulum. 'Even in places where mesenchyme cells are closely connected, no interchange of granules or mitochondria can be observed. These cells thus behave as individual units that are adherent to one another because their surfaces are sticky' (p. 393). In tissue cultures nearly every type of embryonic cell has the power of independent feeding, like a phagocyte, ingesting any particulate matter found in the culture (pp. 424–5).

To take one more example, G. Levi[2] found that:

'In the tissues of the embryo chick syncytia characterized by a complete loss of the biological individuality of the composing cells do not occur. Even the tissues in which the connections between cell and cell are most intimate (myocardium, mesenchyme) show in cultures *in vitro* a protoplasmic activity leading to the migration of single cells into the clot.... Syncytia should therefore be considered as consisting of plasmatic masses or areas which are biologically delimited by the sphere of influence of their nuclei, and though intimately united they still possess, potentially, the capacity of separating from one another.'[3]

Migration of cells as independent units is of quite common occurrence in tissue cultures, and the origin of new cells by division is frequently observed. The single cells can also in many cases be seen to grow and differentiate as individuals. All these points were established by the earliest workers on tissue cultures (Harrison and Burrows)[4] and have been fully confirmed since.

[1] W. H. Lewis and M. R. Lewis, 'Behavior of Cells in Tissue Cultures', in Cowdry, *General Cytology*, Chicago, 1924.

[2] *Arch. exper. Zellforsch.* i, 1925, pp. 1–57.

[3] Abstract in *Journ. Roy. Micr. Soc.*, March 1926.

[4] R. G. Harrison, 'The Outgrowth of the Nerve Fiber as a mode of Protoplasmic Movement', *Journ. Exper. Zool.* ix, 1910, pp. 787–846; M. T. Burrows, 'The Growth of Tissues of the Chick Embryo outside the Animal Body with special reference to the Nervous System', ibid., x, 1911, pp. 63–83.

Harrison's pioneer experiments were carried out on little pieces of tissue isolated from frog embryos of 3–4 mm. in length. He noted that the cells of the medullary cord at this early stage of development, though appearing syncytial in sections, fall apart into quite distinct cells when dissected out fresh. The following quotations are taken from his own summary of results:

'Pieces of undifferentiated embryonic tissue, when isolated under aseptic precautions in clotted lymph, will live for weeks and undergo at least the initial stages of normal histological differentiation; cells from the axial mesoderm give rise to striated muscle fibers; epidermal cells form a cuticular border; typical chromatophores and a mesenchyme-like tissue are formed from pieces containing portions of the neural tube and axial mesoderm; the walls of the neural tube and the primordia of the cranial ganglia give rise to long hyaline filaments closely resembling embryonic nerve fibers' (p. 841).

His most striking observations were those relating to the mode of formation of nerve fibres, which he found to originate as protoplasmic extensions of the medullary nerve cells which grew to a considerable length. Harrison regarded this outgrowth as a manifestation of protoplasmic movement, that is, as an active function of the individual nerve cell.

'One characteristic that the embryonic cells have in common is the power of movement. They change their form or move from place to place in the clot by virtue of the amoeboid activity of their hyaline ectoplasm. . . . In the case of cells from the medullary tube and the primordia of the cranial ganglia the activity is so localized and the ductility of the ectoplasm is such, that the movement results in the formation of long fibers, the primitive axones. The free end of each fiber is enlarged and provided with fine processes or pseudopodia. This part continues its progression and the fiber is gradually drawn out. . . . The longest fiber observed, and this was followed throughout its whole period of growth (53 hours), was 1·15 mm. long' (p. 842).

'The first nerves which form are composed of few fibers and have relatively short distances to grow before establishing connection with their end organs. The long paths found in the adult are largely the result of subsequent stretching or interstitial expansion, which takes place as the various parts grow or shift apart. The fibers which develop later follow, in the main, the paths laid down by the pioneers' (p. 843).

Burrows confirmed Harrison's results on other material, the chick embryo, and clearly established the fact that the growth of the mesenchyme tissue consisted in the wandering out of the pre-existing tissue cells and their multiplication by mitotic division.

It will be apparent that Harrison gives a quite different account of the origin and differentiation of ganglion cells and nerve fibres from that suggested by Rohde. The problem is a very difficult one, and the interpretation to be given to the observed facts about the development of nerve-fibres is still in dispute. Sedgwick, for example, in the paper of 1895 already referred to, took the line that both nerves and muscles were special developments of the primitive reticulum or plasmodium. With regard to nerves he wrote:

'. . . the development of nerves is not an outgrowth of cell-processes from certain central cells, but is a differentiation of a substance which was already in position; and this differentiation seems to take place from the medullary walls outwards to the periphery, both in the anterior and posterior roots, and to precede, or to proceed *pari passu* with, the development of other tissues. The nerve crest is, then, to be regarded as a centre for the growth of nuclei, which spread into the body of the embryo and become concerned in the formation of many tissues, nervous tissues among the rest' (ibid., p. 94).

There is always the possibility that what Harrison observed was not the original, normal formation of the axon fibre, but the regeneration of an intercellular connexion, which had been ruptured when the piece of medullary cord was removed from the embryo.

The results obtained by Graham Kerr[1] in his very careful study of the development of nerves in *Lepidosiren*, a peculiarly favourable subject, on account of the large size of its cells, are difficult to harmonize with Harrison's view.

Graham Kerr concluded from his investigation of the early development of motor nerves in this form that '(1) The nerve-trunk is already present as a protoplasmic bridge at a period so early in development that spinal cord and myotome are still in contact with one another. (2) As the embryo

[1] J. Graham Kerr, *Text Book of Embryology*, vol. ii, London, 1919, pp. 106–21.

grows and the myotome recedes from the spinal cord this protoplasmic bridge increases in length and becomes fibrillated. (3) As the nerve-trunk lengthens amoeboid masses of mesenchymatous protoplasm collect round it and gradually spread out over its length to form the protoplasmic sheath' (p. 110).

Graham Kerr subjects to severe criticism the view originally suggested by His, and apparently confirmed by Harrison's experiments, that nerve fibres are formed by active outgrowths from the central nerve cells. He points out that in Harrison's preparations there may well have been present the original protoplasmic bridges, broken off from their connexion with the myotomes, and that it may have been these nerve-rudiments, appearing as processes of the nerve cells, that exhibited the observed active growth and prolongation.

In general, Graham Kerr agrees with Sedgwick as to the great importance of intercellular connexions, though he points out that these do not seem to exist between the segmentation spheres, and only appear as a secondary formation at a somewhat later stage. He stresses the importance of regarding the individual not as an aggregate of cells and organs, but as a mass of living substance imperfectly subdivided up into subordinate units: imperfectly because each cell and each organ is closely bound up with the activity of the whole organism (p. 487).

The results of tissue-culture work on the whole favour the 'cell-state' theory of the organism, in that they show the individual cell to possess a certain independence of movement and power of differentiation. There may be adduced also in favour of this view the very remarkable evidence brought forward by H. V. Wilson (1907, 1910), Morgan and Drew, and others, indicating that in certain lowly organized animals, such as Sponges and Hydroids, tissue cells artificially dissociated can come together and form a new organism. For an account of this phenomenon in Sponges we may follow the recent full description provided by Galtsoff.[1] For his

[1] P. S. Galtsoff, 'Regeneration after Dissociation (An experimental study on Sponges), I and II. *Journ. Exper. Zool.* xlii, 1925, pp. 183–222 and 223–56.

experiments he used the sponges *Microciona prolifera* and *Cliona cellata*, and these he broke up into single cells and small aggregates by squeezing them through fine-meshed bolting silk. He found that larger aggregates were formed through the amoeboid activity of the archaeocytes (unspecialized, granular mesenchyme cells) which crept about irregularly and collected other cells by adhesion. The archaeocytes are very sticky and collect all the foreign bodies they meet: they will not however pick up cells of another species. The archaeocytes do not fuse into a plasmodium, but adhere in a common hyaloplasm, which may form a large pseudopodium by means of which the aggregate moves. The aggregates are fully formed after 24 hours, and form spheres about 120–50μ in diameter. Each of the aggregates if large enough develops into a sponge possessing a single osculum.

'Large aggregates develop faster and live longer than the small ones. A complete regeneration occurs in aggregates consisting of about 2,000 cells or more. The aggregates composed of a small number of cells, from about 40 to 500, fail to develop into perfect sponges: their canals do not fuse into one system and the osculum is frequently wanting (p. 250). The re-formation of a new sponge is primarily brought about by the coming together of cells, followed by their further differentiation. Increase in the number of cells takes place after the sponge body is formed. The rebuilding of the new sponge is then due 'to the activities and properties of individual cells forming an aggregate. The different types of cells forming a common mass find each other and then develop flagellated chambers, canals, skeleton, mesenchyme, and other tissues'.

A similar collaboration of dissociated cells, leading towards the formation of a new organism, was observed in *Antennularia* by Morgan and Drew,[1] but here the process of reformation was not so complete. The experimental procedure was the same as in the Sponge work, and as a result of dis-

[1] W. de Morgan and G. H. Drew, 'A Study of the Restitution Masses formed by Dissociated Cells of the Hydroids *Antennularia ramosa* and *A. antennina*', *Journ. Mar. Biol. Assoc.* x, 1913–15, pp. 440–63.

sociation isolated cells and small groups were obtained, which aggregated together to form compact masses. A perisarc was formed by these masses, and a definite layer of ectoderm surrounding a plasmodial mass of endoderm, in which coenosarcal tubules developed, similar to those in the normal hydroid. Hydranths were however not formed during the course of the experiment, which was continued for 60 days. There was no sign of any multiplication of cells by division.

These results, especially in Sponges, are certainly of great value and significance, and show that in such forms the tissue cells, even when differentiated, still retain a considerable measure of independence, enabling them to co-operate in a most remarkable and orderly way in building up, either completely or partially, a new organism; but it must be remembered that the Sponges, in which alone a complete regeneration of typical form was achieved, are a group of peculiar organization, resembling much more closely a colonial aggregation of cells than do the higher Metazoa, and that they do normally form restitution bodies in the shape of *Gemmules*.

5. We have now seen in broad outline what kind of evidence is adduced in favour of their view by the upholders of the plasmodial and the cellular theory of the organism respectively. We may properly draw the conclusions—(1) that the evidence is to some extent conflicting, (2) that neither view expresses the whole truth, and (3) that both contain part of the truth. Plasmodia and independent cells do certainly both exist, and it is probable that in the early stages of histogenesis a plasmodial or syncytial type of structure is more widely spread than the cell-theory would have us suppose. Certain it is that the dictum *Omnis cellula e cellula* is of less wide application than the aphorism *Omnis nucleus e nucleo*, which appears, unlike the other, to be strictly true and to admit no exception.

But the question as to whether or not cells are distinct morphological entities is in no way crucial or fundamental for our interpretation of the relation between the organism and its cells. We have considered the question too

exclusively from the morphological point of view and we must now look at it from the standpoint of physiology. As D'Arcy Thompson writes:

'Discussed almost wholly from the concrete, or morphological point of view, the question has for the most part been made to turn on whether actual protoplasmic continuity can be demonstrated between one cell and another, whether the organism be an actual reticulum or syncytium. But from the dynamical point of view the question is much simpler. We then deal not with material continuity, not with little bridges of connecting protoplasm, but with a continuity of forces, a comprehensive field of force, which runs through and through the entire organism and is by no means restricted in its passage to a protoplasmic continuum. And such a continuous field of force, somehow shaping the whole organism, independently of the number, magnitude and form of the individual cells, which enter, like a froth, into its fabric, seems to me certainly and obviously to exist.'[1]

Physiologically, the organism is a unity and acts as such. Whether it is composed of more or less discrete cells, or is essentially continuous in substance, makes no difference to this unity of action. Intercellular bridges are not the only means at disposal to ensure co-ordination of action. The nervous system is obviously the main channel and organ through which the general integration of activity is achieved and maintained; the *milieu interne*, which bathes all the living parts of the body and serves as the vehicle for hormones and other dissolved substances, is also of great importance as a means of integration.

Integrative or 'whole' action means that the activities of the parts are subordinated to the activity of the whole. Cell-activities are carried out essentially 'for the good of' the whole organism, and cells and energids are therefore subordinate parts, or organs in the most general sense. Their activities are not to be fully understood save in relation to the general activity of the organism. They are as a rule specialized for particular functions, in accordance with the principle of division of labour, and they are incapable of long-continued existence apart from the particular con-

[1] *On Growth and Form*, p. 200.

ditions which they find in the organism of which they form part. It is true that cells in tissue-cultures may live and multiply for years, but this is only because the conditions in which they normally live are artificially reproduced and steadily maintained over long periods of time. Certain free-moving cells of the Metazoan body, for instance the leucocytes of oysters, can also exist for considerable periods apart from the body, but not indefinitely.

The tissue cell, then, is always physiologically a *part*, and never in normal circumstances a *whole*.

6. We have seen reason to conclude that the main object of the wellnigh universal *nucleate* organization of living things is to maintain a spatially close association between nuclear and cytoplasmic substance, and we have seen that this intimate relation is necessary for constructive metabolism and growth. This interpretation of the facts we have called the energid conception of the organism. The formation of discrete and differentiated cells is something superadded to the primary energid organization, and it appears to be a necessary pre-condition for any great elaboration of structure and any great increase in size. But the fact that histological differentiation affects primarily the cytoplasm, while the nucleus remains as a rule uniform in structure, suggests that the nuclei are there, scattered throughout the substance of the organism, primarily for their original metabolic purpose, that of rendering possible organic synthesis and growth. They may have nothing to do directly with cellular differentiation beyond supplying the necessary conditions for the continued existence and development of the cells or areas of cytoplasm with which they are associated. There is of course no fundamental difference physiologically between the energid and the cell. In the polyenergid non-cellular organism each nucleus has its own zone of influence, of restricted size; it is easy to imagine how from this physiological separation there might develop a more or less complete morphological separation, and cells be formed, either multinucleate or uninucleate. As Rohde points out, we can see this evolution taking place before our eyes in the *Siphonocladaceae*.

The energid conception of the organism is therefore applicable not only to plasmodial organisms but also to such as are fully cellular.

7. In multinucleate organisms, each nucleus with its associated zone of influence, whether it is separated off as a cell or not, must be regarded as a subordinate part or organ of the whole—it is not an independent whole, and cannot be regarded as a self-existent unit, save by abstracting from its relations with the whole.

This summary statement of the conclusions we have reached in this and the preceding chapter brings us back to the two laws of biological method which we formulated in Chapter IX. Since in multinucleate organisms both the energid and the cell are to be regarded as parts and not as wholes, their relations to the whole must be treated in accordance with these two laws.

The first law, which states that the activity of the whole cannot be fully explained in terms of the activities of the parts, runs definitely counter to the classical cell-theory. This theory asserts that all multicellular organisms are built up of fundamental units, the cells, as a house is built of bricks or stones. It asserts further that the activity of the organism as a whole is a summation or resultant of the activities of its component cells: the cell—not the organism—is regarded as the real unit, both morphologically and physiologically.

The theory is in fact a typical product of the method of analytical abstraction, the limitations and dangers of which we have studied in Chapter IX. Against the cell-theory in its classical form the following considerations must be adduced. There is a unity of the whole organism—it develops as a whole, and acts as a whole—and this unity is not a secondary or composite thing, but primary and original. To distinguish cells as independent unities, having their own modes of action independent of the action of the whole, is to regard them abstractly, and to introduce an artificial simplification. From such abstract elements it is impossible fully and completely to recompose the original unity from which they have been separated out by analytical abstraction. We shall see in

more detail in the next chapter that in actual demonstrable fact the ovum and the embryo are from the very beginning unitary organisms—that the unity of the organism is not something which comes to be during the course of development, but is there *ab initio*. We shall see that the importance of cell-formation in development has been greatly overemphasized, to such an extent indeed that the primary unity of the developing organism from the egg onwards has been almost lost from sight.

Our second law, that the activities of the parts cannot be fully understood save in relation to the activities of the whole, gives us the essential rule for the interpretation of cell-activities. These must always be interpreted in relation to the general activities of the organism, as playing their part in one or other of the master-functions of the organism—maintenance, development, and reproduction.

From the organismal point of view, which is implicit in these two laws, the cells taken separately no more constitute the organism than words and letters by themselves make a sentence—the unity and the meaning are in the respective cases prior to the components.

It may be well to make quite clear once more that the organismal conception merely gives rules of method for the study of living things and their parts, that it implies no mysterious 'action of the whole' on the parts. There is no internal controlling agency which acts in a mysterious way to bind up the parts into a whole, no separate entelechy, either material or immaterial, which guides and controls organic processes. We accept the simple facts of observation that the organism acts as a whole, and that the activities of its parts are subordinated to, and co-operate in, whatever the organism as a whole is doing at the moment of observation. It is from this simple and objective standpoint that we must regard the relation between the organism and its cells and energids.

8. In conclusion, we may briefly consider the relation of unicellular organisms to the cell-theory. In our discussion of the energid theory of the organism we came to the provisional conclusion that the primary difference between

monoenergid and polyenergid organisms must be one of size. We shall see in what follows that this view is essentially correct, that the unicellular animal or plant is primarily an organism, comparable with the whole of a Metazoan or Metaphytan body, and only secondarily a cell, and that by reason of its small size. Unlike the tissue cell the unicellular organism is a whole and not a part. It can be compared with a tissue cell only in respect of an incidental likeness—the fact that it is, as a rule, monoenergid.

This thesis as to the nature of unicellular organisms is so obvious as hardly to require elaboration. The fact that these forms live and develop and reproduce as individuals is quite enough to show that they must be regarded primarily as organisms, and only incidentally as cells. But the influence of the cell-theory has been powerful enough to obscure this obvious conclusion; it has led to the unicellular organism being regarded as the equivalent of the tissue cell of the higher forms, and to the Metazoon being looked upon as a colony of differentiated cells, each homologous with a Protozoon.

So long ago as 1883 Rauber protested against this abstract and morphological view, and maintained that on the contrary the Protozoon was to be homologized with the whole body of the Metazoon. The essential difference between them was that the Protozoon had only one surface, the external surface of the body, while the Metazoon possessed, in addition to an external surface, many internal cell-surfaces. In the unicellular organism the cell *is* the whole (1883, p. 332). He denied that the tissue cell was an 'elementary organism', or the Metazoon a composite assemblage of independent units. Both the Protozoon and the Metazoon were essentially *wholes*.

In more recent days, as a result of the modern development of 'Protistology', several workers in this field have emphasized the direct homology of unicellular and multicellular organisms, and pointed out the inadequacy of regarding the former as simple cells. In particular Dobell[1] has made a

[1] C. Clifford Dobell, 'The Principles of Protistology', *Arch. f. Protistk.*, xxiii, 1911, pp. 269–310.

vigorous onslaught upon the cell-theory in its application to the Protista. By Protista he means Protozoa, Protophyta, and such other 'unicellular' forms as cannot be definitely allotted to either group.

He maintains that the Protista are organized upon quite a different principle from other living things. They are not really 'cellular', for according to Dobell a 'cell' is always a *part* of an organism, and Protista are whole organisms. 'An absolutely fundamental point', he writes, 'is this: one whole protist individual is a complete individual in exactly the same sense that one whole metazoan individual is a complete individual. Amoeba is an entire organism in just the same sense that man is an entire organism . . . it is clear that a protist is no more homologous with one cell in a metazoon than it is homologous with one organ (e.g. the brain or liver) of the latter' (p. 272). Again, 'I would emphasize the fact . . . that a protist behaves as a whole organism, and not as a part of one, and a metazoon behaves as a whole organism in just the same way, and not as a "colony" or "state" of separate individuals' (p. 273).

In sum, Protists are not primitive and simple organisms. 'The truth . . . is that the Protista are very small—but they are not simple. In them, we do not see vital processes in a more elementary form than in other organisms: we see them rather in a more complex form—due to what may be called the "multum in parvo" principle on which all Protista are organized' (p. 307). That the Protista are all small is, as we have seen, easily explained by the fact that they are (with some exceptions) monoenergid.

One thing has emerged very clearly from the modern intensive investigation of Protista, and that is the amazing complexity of organization which can be developed within the confines of a single cell. This is noticeable particularly in Ciliates, and suggests that Ehrenberg was nearer the truth when he ascribed organs to the Infusoria than were his successors who saw in the Protozoa merely nucleated masses of unformed protoplasm. As an example of a high degree of intracellular organization, let us take

Diplodinium ecaudatum, whose structure is thus described by Calkins:[1]

'Bars of denser chitinous substance form an internal skeleton; special retractile fibers draw in a protrusible proboscis; similar fibers closing a dorsal and a ventral operculum; other fibrils, functioning as do nerves of Metazoa, form a complicated coordinating system; cell mouth, cell anus, and a fixed contractile vesicle or excreting organ, are also present. All of these are differentiated parts of one cell for the performance of specific functions, and all perform their functions for the good of the one-celled organism which measures less than 1/250 inch in length. Analogous, if not so complete intracellular differentiations are present in the majority of Infusoria, while many of the flagellates, notably the Trichonymphidae, have an almost equally elaborate make-up' (p. 19).

Functionally these organellae correspond to the organs of the Metazoon, and the fact that they are intracellular, instead of being composed of differentiated cells, should not hide from us their essential similarity with organs: the difference is primarily one of scale or dimensions. Calkins, like Dobell, holds that the Protozoa are more satisfactorily regarded as organisms than as cells: 'as organisms the Protozoa are more significant than as cells. In the same way that organisms of the metazoan grade are more and more highly specialized as we ascend the scale of animal forms, so in the Protozoa we find intracellular specializations which lead to structural complexities difficult to harmonize with the ordinary conception of cells' (p. 19).

The distinguished Russian protozoologist Awerinzew,[2] in a paper on the systematic position of the Protozoa, has also called attention to the close analogy between the intracellular differentiations of the higher Protozoa and the specialized tissues and organs of the Metazoa. We may conveniently conclude this chapter by quoting his considered opinion that between the Protozoa and the Metazoa there exists no qualitative, but only a quantitative difference (p. 466).

[1] G. N. Calkins, *The Biology of the Protozoa*, London, 1926.

[2] S. Awerinzew, 'Ueber die Stellung im System und die Klassifizierung der Protozoen', *Biol. Centrbl.* xxx, 1910, pp. 465–75.

XIII

THE CELL IN RELATION TO DEVELOPMENT AND DIFFERENTIATION

LIKE the Protozoon, the animal ovum is by definition a cell, but—also like the Protozoon—it is in addition an organism and not merely a cell. It is the organism in its earliest stage, when it is small and monoenergid. When the ovum segments it still remains one organism, with the sole change that it has become polyenergid, and as a rule multicellular. There is direct continuity from the unsegmented ovum right up to the adult organism. It is true that in many cases the segmentation-spheres appear to be spatially distinct,[1] and single blastomeres may have the power when isolated of reproducing the whole organism. But there are also many cases, e.g. in Arthropods, where separate blastomeres are not formed at first, and the embryo remains for some time plasmodial.

Under the influence of the cell-theory, the simple fact of organic continuity from ovum to adult has been rather overlooked, and too much stress laid on the multiplication of cells during early ontogeny. It has been considered that segmentation is essentially a process of duplication and re-duplication of that which is accepted as the fundamental biological unit —the cell, and that differentiation is based upon cell-multiplication.

It is to Rauber[2] in 1883 that we owe the restatement of the obvious truth that in spite of cell-multiplication the organism is and remains one unity from the earliest to the latest stages of its development, and that accordingly the unsegmented egg is not merely a cell but a unicellular or monoenergid organism.

The living thing is not constructed as is a house or a factory, by the adding together in an orderly way of one

[1] Intercellular connexions between blastomeres have been observed in echinoderm and nemertine eggs (Refs. in Wilson, 1925, p. 106).

[2] *Morph. Jahrb.* viii, 1883, pp. 233–338.

building-stone after another; its unity and primary plan are there from the beginning, so that the organism is from the beginning a whole, from which by self-differentiation the parts are derived[1] (p. 308). In this sense the whole determines the parts, not the parts the whole.

'For the finished organism is nothing else than the fertilised egg which has increased and divided in an orderly way. The determining conditions of the type of growth are contained in the egg, as are also those of its division. The fertilised egg is the whole in its youngest state. The first two segmentation spheres, into which it divides, derive all that they are from their source, the egg. What is true for the first two parts holds good for all the rest—they are determined according to the laws which presided over their first beginnings' (pp. 313–14).

From which we get the following definition of the developing organism: it is 'a protoplasmic body which increases in size in definite directions, divides itself up in the different dimensions of space, and differentiates itself in orderly fashion chemically and histologically' (p. 332). The cells into which it divides are of subsidiary and minor importance in comparison with the developing organism as a whole, and they are in no sense elementary units, or 'elementary organisms'.

In the same year as Rauber, Sedgwick wrote with reference to the syncytial development of *Peripatus*, 'if these facts are generally applicable embryonic development can no longer be looked upon as being essentially the formation by fission of a number of units from a single primitive unit, and the co-ordination and modification of these units into a harmonious whole. But it must rather be regarded as a multiplication of nuclei and a specialization of tracts and vacuoles in a continuous mass of vacuolated protoplasm'.[2] Sedgwick accordingly, like Rauber, took the organismal rather than the analytical view of development.

The same point of view was brilliantly stated by Whitman[3]

[1] The parts are the way in which the whole organizes itself—a phrase which I owe o Mr. R. G. Collingwood (*in litteris*).

[2] Quoted in his paper of 1885, already referred to.

[3] C. O. Whitman, 'The Inadequacy of the Cell-Theory of Development', *Wood's Holl Biological Lectures for 1893*, Boston, 1894, pp. 105–24.

in his famous lecture on the cell-theory. He maintained, and supported his contention with a wealth of illustration, that the organization of the embryo and the adult is independent of the manner of its subdivision into cells. 'The plastic forces heed no cell-boundaries, but mould the germ-mass regardless of the way it is cut up into cells' (p. 110). The organism is an organism from the egg onwards, and *continuity of organization* is the essential thing in development, division into cell-territories being entirely secondary. 'Continuity of organization does not of course mean preformed organs, it means only that a definite structural foundation must be taken as the starting-point of each organism, and that the organism is not multiplied by cell-division, but rather continued as an individuality through all stages of transformation and subdivision into cells' (p. 112).

With this typical organismal or integral view of development he contrasts the colonial, elementalist conception, which was then widely held.

'While all will admit that the organization of the egg is such as to predetermine the organism, few will be prepared to admit that the adult organization is identical in its *individuality* with that of the egg. The organism is regarded rather as a community of such individualities, bound together by interaction and mutual dependence. According to this view, development does not consist in carrying forward continuous changes in the same individual organization, but in multiplying individualities, the complex of which represents, at every stage, not *the* organism, but one of an ascending series of organisms, which is to terminate in the adult form.'[1]

'In the egg-cell we are supposed to have an elementary organism; in the two-cell stage, two elementary organisms, forming together an organism of a totally different order, based on a new scheme of organization. In the four-cell stage we have another organism, in the eight-cell stage another, and so on' (pp. 113–14).

This view, he holds, is totally incorrect. The unity of the

[1] That this is not an exaggerated statement of the elementalist position is shown by the following passage quoted in translation from Hertwig by E. B. Wilson (*Wood's Holl Biological Lectures for 1893*, p. 8): 'The egg is an organism which multiplies by division to form numerous organisms equivalent to itself, and it is through the interactions of all these elementary organisms, at every stage of the development, that the embryo, as a whole, undergoes progressive differentiation.'

organism is not a secondarily acquired unity, it is there from the beginning of development—fundamental organization precedes cell-formation in time and regulates it, rather than the reverse.

'We must look entirely behind the cellular structure for the basis of organization. Even a highly differentiated organism may reach a relatively late stage of development just as well without cell-boundaries as with them, as we see so well illustrated in the insect egg. If we fall back on the number of nuclei as the essential thing, then we shall have to reckon with multinucleate infusoria. In these forms do we not see that it is always the same organism before us, as we follow its history through the whole cycle of nuclear phases?

'The essence of organization can no more lie in the number of nuclei than in the number of cells. The structure which we see in a cell-mosaic is something superadded to organization, not itself the foundation of organization. Comparative embryology reminds us at every turn that the organism dominates cell-formation, using for the same purpose one, several, or many cells, massing its material and directing its movements, and shaping its organs, as if cells did not exist, or as if they existed only in complete subordination to its will, if I may so speak' (p. 119).

It is a curious fact, to be explained no doubt by the strength of the particulate conception in his time, that Whitman considered the ground of assimilation, reproduction, and regeneration, in short of all the fundamental vital functions, to lie in ultra-microscopic idiosomes, whose action and control were of course not limited by cell-boundaries (p. 123). The idiosomes were the bearers of heredity and the real builders of the organism—the determining agents of organization and differentiation. But clearly, organization can no more be explained by the properties of the individual idiosomes than the unity of the organism can be explained from the properties of its constituent cells.

If Whitman had applied to the idiosomal conception the same criticism which he used with such effect against the cell-theory, he would have been convinced of the total inadequacy of this conception also.

Dobell, in the paper to which we referred in the last chapter, contrasts the segmentation of the Metazoan ovum

with the multiplication of the Protozoan individual. He writes:

'A metazoan egg undergoing segmentation is a non-cellular organism undergoing differentiation by forming cells. Before segmentation the egg is a whole organism; after segmentation it is *the same* whole organism, but more differentiated. After segmentation, the organism is *not* a colony of individuals each of the same value as the original egg. A protozoon undergoing division, on the other hand, is one organism dividing into two; it is one whole organism becoming two whole organisms of the same value as the original whole organism. If segmentation were really analogous to the divisions of a protozoon, it would produce a cluster of eggs and not a differentiated organism' (p. 302).

In stating recently the fundamental concepts of the physiology of development, F. R. Lillie [1] gave a prominent place to the principle of 'individuation'.

'The germ', he wrote, 'is physiologically integrated as an individual at all stages. It may be first merely a cellular individual, then a definitely polarized individual with one or more axial gradients; as development proceeds, specific correlations, including those of definitely nervous and chemical natures, make their appearance. In short, the physiological principles upon which integration depends undergo differentiation, in the sense of progress from relatively simple and few to relatively complex and many, during development. While individuality may thus *appear* to grow, it is in reality complete at all stages, only the means to its realization changing and multiplying with growing complexity' (p. 362).

A good example of the organismal conception of development! Lillie expressed this same view of the essential unity of the developing organism even more clearly in an important paper written some twenty years previously,[2] in which the following striking passage occurs:

'If any radical conclusion from the immense amount of investigation of the elementary phenomena of development be justified, this is; that the cells are subordinate to the organism, which produces

[1] 'The Gene and the Ontogenetic Process', *Science*, lxvi, 361–8, 1927.

[2] 'Observations and Experiments concerning the Elementary Phenomena of Embryonic Development in *Chaetopterus*', *Journ. Exper. Zool.* iii, 1906, pp. 153–268.

them, and makes them large or small, of a slow or rapid rate of division, causes them to divide, now in this direction, now in that, and in all respects so disposes them that the latent being comes to full expression. We see this in the adaptiveness of the process of cleavage of the ovum, in the regeneration of a starving planarian constantly suffering a diminution in the number of its cells while its structure is increasing in complexity, in "regulation", and in all cases of morphallaxis, whether in a protozoan or a metazoan. The organism is primary, not secondary; it is an individual, not by virtue of the cooperation of countless lesser individualities, but an individual that produces these lesser individualities on which its full expression depends' (p. 252).

This principle of unity, or action of the organism as a whole, corresponds to Whitman's concept of organization. It is prior to visible differentiation, and is a 'property of the whole distinct from the discernible properties of the parts' (p. 253).

The same view, that development is essentially an activity of the organism as a whole, has also been upheld by others—by Conklin and Child for instance, and by Ritter, as we have seen in earlier chapters.

2. The argument from the continuity of development is sufficient in itself to show that the ovum is not merely a cell but the future organism in its simplest state. But there is in addition a good deal of evidence which indicates that in many groups the fertilized but unsegmented egg is already differentiated as a whole, in such a way that particular areas of its substance represent and give rise to particular organs and organ-systems of the adult—I refer of course to the facts of 'germinal localization'. We shall see more clearly in considering these facts that development is essentially a process affecting the organism as a whole, that the organism develops as a unity from its earliest beginnings right up to maturity and old age, and that cell-division and even nuclear division are events ancillary and adjuvant to the main developmental process, not primary and fundamental events in terms of which that process can be fully expressed.

We shall see that the ovum is essentially a monoenergid organism which differentiates its substance progressively, and

becomes by reason of its increase in size polyenergid, and as a rule multicellular. The story of early development, as revealed by the able experimenters of the last thirty years, provides us in fact with a clear demonstration of the necessity for a synthetic or organismal treatment of development, and of the complete inadequacy of the analytic view.

It is to W. His in 1874 that we owe the first suggestion of organ-forming areas in the germ (see above, p. 95 f.n.), but the seed fell on stony ground, and was stifled by the upgrowth of speculation on the part played by the nucleus in differentiation, which followed the brilliant cytological discoveries of the early '80s. Experimental embryologists, under the influence of the cell-theory, at first paid attention chiefly to the fate of isolated blastomeres and groups of blastomeres, and it was not till near the end of the century that they discovered the existence of 'organ-forming substances' located in definite areas of the egg-cytoplasm. Some years later, the theory of germinal localization took shape, particularly from the hands of Wilson and Conklin.

It is unnecessary here to follow up the steps by which the theory was established, the more so because the whole fascinating story is told by Wilson with a competence and authority that cannot be rivalled.[1] For our purpose it is sufficient to single out a few typical cases in support of our contention that the egg is already at a very early stage the organism-to-be.

In the first place we may recall those cases where the egg shows the same orientation and symmetry as the future organism. This is true of many insect eggs, which have an anterior and a posterior end, dorsal and ventral surfaces, and a right and left side, which correspond with these aspects in the adult. The egg of the cuttlefish, *Loligo*, also shows definite bilateral symmetry.

For more detailed evidence of germinal localization we must however turn to those eggs that exhibit 'mosaic' cleavage, of which many examples are known among Mollusca, Annelida, and Ascidians. As a typical case we may take the

[1] Wilson, 1925, Chapters XIII and XIV.

ascidian *Styela*, so thoroughly investigated by Conklin. In the egg of *Styela* germinal localization is not established until maturation and fertilization take place. In the egg before maturation there is visible only a central grey yolky mass, surrounded by a superficial layer containing yellow pigment. When the germinal vesicle breaks down to form the first polar spindle, a clear substance is liberated which later forms the ectoderm of the larva. Further localization is dependent on the entrance of the sperm. When this happens, the yellow superficial plasm collects at the lower pole of the egg, where the sperm enters, forming a yellow cap.

'This yellow substance then moves, following the sperm nucleus, up to the equator of the egg on the posterior side and there forms a yellow crescent extending round the posterior side of the egg just below the equator. On the anterior side of the egg a gray crescent is formed in a somewhat similar manner, and at the lower pole between these two crescents is a slate blue substance, while at the upper pole is an area of colorless protoplasm. The yellow crescent goes into cleavage cells which become muscle and mesoderm, the gray crescent into cells which become nervous system and notochord, the slate blue substance into endoderm cells and the colorless substance into ectoderm cells. Thus within a few minutes after the fertilization of the egg, and before or immediately after the first cleavage, the anterior and posterior, dorsal and ventral, right and left poles are clearly distinguishable, and the substances which will give rise to ectoderm, endoderm, mesoderm, muscles, notochord, and nervous system are plainly visible in their characteristic positions.'[1]

The monoenergid egg of *Styela* is therefore, immediately after fertilization, a rough model of the future organism; its subsequent development consists in a further differentiation of the organ-systems already mapped out, accompanied by an increase in size.

While in *Styela* and in many other forms definite localization of special cytoplasmic areas does not take place before fertilization, it is to be noted that this is not an invariable rule. In some forms, e.g. *Myzostoma* and *Dentalium*, a definite zoning of 'formative substances' is established even

[1] E. G. Conklin, *Heredity and Environment*, 2nd edit., Princeton, 1916, pp. 123–4.

before maturation. As Wilson points out, the history of development does not commence with fertilization—there is an epigenetic differentiation of the ovarian egg, leading up to the stage at which it can be fertilized, or otherwise stimulated to begin the development of a new organism.

While the Ascidian is the type in which germinal localization is most detailed and most clearly visible, the state of affairs which we have described for *Styela* is parallelled in greater or less degree in most of the great groups of the animal kingdom.

'There are types of localization of these cytoplasmic materials in the egg which are characteristic of certain phyla; thus there are the ctenophore, the flat-worm, the echinoderm, the annelid-mollusk and the chordate types of cytoplasmic localization. The polarity, symmetry and pattern of a jellyfish, starfish, worm, mollusk, insect or vertebrate are foreshadowed by the characteristic polarity, symmetry and pattern of the cytoplasm of the egg either before or immediately after fertilization. In all of these phyla eggs may develop without fertilization, either by natural or by artificial parthenogenesis, and in such cases the characteristic polarity, symmetry and pattern of the adult are found in the cytoplasm of the egg just as if the latter had been fertilized' (Conklin, ibid., pp. 181–2).

For our second example we may take the egg of the frog, which shows, immediately after fertilization, a structure foreshadowing that of the adult, though not visibly in such detail as does the egg of *Styela*. We shall follow the admirable account given by Brachet,[1] who has himself contributed so much to the elucidation of the first steps in the development of this much studied form.

In the ripe but unfertilized egg of *Rana fusca* (=*R. temporaria*) there is no trace of bilateral symmetry. There exists of course a radial symmetry, and a differentiation of the animal from the vegetative pole. Such polar symmetry is almost universal in animal ova, and has as a rule a very definite prospective significance, since the substance of the animal pole generally gives rise to the ectoderm and its derivatives, that of the vegetative pole to the endoderm. In

[1] A. Brachet, *L'Œuf et les Facteurs de l'Ontogénèse*, Paris, 1917.

the egg of *Rana*, before fertilization, there is no specific localization of potentialities; destruction of a small area of the cytoplasm of the egg does not lead to a specific defect in the embryo, provided the operation is carried out before, or shortly after, fertilization. Up to about 45 minutes after fertilization, germinal localizations either do not exist, or if they have been formed, they are unstable and labile, and the egg can still regulate and re-arrange them. When more than an hour has passed, local injury to the cytoplasm entails the absence in the embryo of the part to which this locus of the cytoplasm normally gives rise—the egg has become definitely and irrevocably a mosaic of potentialities of a generalized character. This organization and fixation of elementary structure is in the frog normally brought about by the entrance of the sperm, and reaches its term at the moment when fusion of the male and female pronuclei takes place. About two hours after fertilization a visible external sign of the organization of the egg becomes apparent in the shape of the grey crescent, which forms at one side between the pigmented upper hemisphere and the lower white hemisphere. The grey crescent is invariably directly opposite the point of entrance of the sperm; it marks the plane of bilateral symmetry which is now established in the egg; and this plane becomes invariably the plane of symmetry of the embryo and the adult. The dorsal lip of the blastopore, which acts as a centre of growth and differentiation, takes its origin from the broadest part of the crescent.

We see then that shortly after fertilization the main lines of the future organization are laid down in the unsegmented egg.

When the egg is artificially fertilized, as can be done by pricking it with a needle, the formation of the grey crescent takes place normally, and the egg organizes its structure, though there is no relation between the position of the prick and the point of appearance of the grey crescent. The establishment of bilateral symmetry and of the main lines of organization is then clearly independent of any specific organizing action of the male pronucleus.

The localization of specific potentialities in the unsegmented egg of *Rana* is not so detailed and definite as in *Styela*, or at least is not so easily demonstrable; the frog's egg therefore occupies an intermediate position between typically mosaic eggs and the so-called regulative eggs, in which germinal localizations are much less definite and much less stable. As an example of the regulative type we may take the egg of the sea-urchin *Paracentrotus* (*Strongylocentrotus*) *lividus*, investigated by Boveri. This egg shows a horizontal band of pigment lying below the equator, separating the top white hemisphere from a bottom white cap. The upper hemisphere gives rise to ectoderm, the pigmented zone to the archenteron, and the bottom cap to mesenchyme. But the separation of the three substances is not very strict, as is shown by the potency of the isolated blastomeres. The first two divisions are meridional, and all four blastomeres receive samples of the three strata of the egg. Each of these four blastomeres when isolated gives rise to a complete larva. The third cleavage plane is equatorial, and establishes a difference between the upper and the lower quartet of cells. In spite of this, however, gastrulae can be obtained from the isolated cells of this stage, but less frequently and less completely from the cells of the upper quartet. The egg showing the least degree of cytoplasmic localization is that of the hydromedusan studied by Zoja, which shows a concentric grouping of substances, such that each of the first sixteen blastomeres receives an equal share, and is accordingly able to produce when isolated a complete small larva. In these eggs, as in the sea-urchin's, bilateral symmetry and the main plan of the future organization are established at a later stage than in the more precocious eggs of *Styela* and *Rana*.

3. We may now consider the relation of cleavage or segmentation to the egg-pattern in these different types. We note, first of all, that at least up to the blastula or corresponding stage, the process of cleavage adds nothing to the original organization of the egg—it merely divides up the substance of the egg in a more or less stereotyped way. In the blastula the same differentiated cytoplasmic regions can

be discerned, occupying the same positions relative to one another as in the unsegmented egg.[1] The localization of substances is the same in the blastula as in the fertilized ovum.

The relation of the cleavage-pattern to the fundamental organization of the egg is different however in the various typical forms we have considered. In *Styela* the cleavage-pattern is modelled upon the egg-pattern, following it closely in such a way as to separate off progressively the differentiated substances of the egg-cytoplasm.

'At the first cleavage of the egg each of these substances is divided into right and left halves. The second cleavage cuts off two anterior cells containing the gray crescent from two posterior ones containing the yellow crescent. The third cleavage separates the colorless protoplasm in the upper hemisphere from the slate blue in the lower. And at every successive cleavage the cytoplasmic substances are segregated and isolated in particular cells, and in this way the cytoplasm of the different cells comes to be unlike. When once partition walls have been formed between cells the substances in the different cells are permanently separated so that they can no longer commingle' (Conklin, 1916, p. 125).

In such typically mosaic eggs, the first cleavage plane stands in a fixed relation to the plane of bilateral symmetry, and the subsequent cleavages separate off progressively the specific areas already differentiated in the cytoplasm of the egg. It comes about then that from the very beginning the individual blastomeres are different from one another, each being specialized for a particular destiny. They are in a measure like tissue cells—specified as to type and fate. We can understand therefore why, if one of the first two blastomeres is killed, the surviving one develops into a half embryo, and not a whole one, and why cells isolated at a later stage (as can be done in the mosaic eggs of some Gastropods) produce only that part of the larva to which they would have given rise normally. The classical case is that of the Ctenophore *Beröe*, in which isolated blastomeres of the 2-cell, 4-cell, or 8-cell stages produce partial larvae,

[1] In illustration of this, see for example Figs. 512 and 513 in Wilson, 1925, and Figs. 6, 9, 10, and 27–9 in Conklin, 1916.

fractions of the whole, possessing respectively 4, 2, or 1 of the normal 8 swimming-combs. The same type of result can be obtained by operating on the unsegmented egg—larvae showing specific defects are obtained.

The relation of cleavage to egg-pattern in the frog's egg is particularly interesting. Here the first cleavage plane may, or may not, coincide with the plane of bilateral symmetry established by the entrance of the sperm. In about 70 per cent. of cases it coincides roughly with the plane of egg-symmetry; exact coincidence is found only in 40–50 per cent. of cases according to Brachet. The two planes may in fact form any angle with one another, but there is a distinct bias towards coincidence. If one of the first two blastomeres is killed the remaining one gives rise to a partial embryo, and the composition of this partial embryo depends upon the relation of the first cleavage plane to the bilateral plane of the egg. If the two planes approximately coincide the result will be a half embryo—right or left as the case may be. If the first cleavage runs transversely across the egg, and the posterior blastomere is destroyed, the anterior blastomere gives rise to an embryo complete as to its front half but dwindling off towards the tail. In general, the fate of the surviving blastomere depends upon how much of the grey crescent it contains (Brachet). The interesting point for us is that there is no necessary relation between the direction of the cleavage planes and the fundamental structural plan of the egg. As Brachet puts it, 'In the fertilized egg of the frog, whatever may be the orientation of the first cleavage plane relatively to the plane of bilateral symmetry, the latter maintains itself completely throughout the whole course of development; all the parts and all the primordial organs of the embryo are formed in positions determined by the material and dynamical constitution of the egg' (1917, pp. 266–7).

We must note in passing that though in the frog as a rule only partial embryos appear after the destruction of one of the first two blastomeres, it is possible by suitable manipulation to obtain a whole embryo of small size from each of the two—the mosaic character of the egg is not so rigid as in *Styela*.

Turning now to the egg of *Paracentrotus*, we find that the germinal localizations are not so precise and stable as in *Styela* and the frog. The symmetry of early development is radial, and the main differentiation is polar. As we have already seen, the first four blastomeres when isolated can give rise to complete larvae, and the same holds good to some extent for the first eight.

It is now generally accepted that the difference between 'mosaic' eggs and 'regulative' eggs is no absolute one, but depends (1) upon the degree of cytoplasmic differentiation reached by the time the egg is capable of fertilization, and on the degree of organization imposed upon the egg by fecundation, and (2) upon the varying regulative power of the egg, which enables a part of it to re-arrange its structure so as to produce not a part but a complete larva of reduced size. Eggs such as that of *Styela* are, as it were, precociously advanced at the time of fertilization, and it is a fact of much significance that with this good start they run through their larval development with great rapidity, reaching the fully formed 'tadpole' stage in 12 hours. Correlated with a highly developed mosaic character of the egg there is generally a lack of regulative power, so that parts of the egg give rise only to partial embryos. The frog's egg is not so advanced in development and has farther to go after fertilization; it has a certain degree of regulative capability. The sea-urchin egg is less advanced still, and quite small fractions of it can reconstitute the whole. It must be remembered that the development of the egg does not begin with fertilization; there is a long period of ovarian growth, during which there is not only a nuclear but also a cytoplasmic maturation. Having regard to the occurrence of natural parthenogenesis and the comparative ease with which artificial parthenogenesis can be induced, we may regard fertilization as an incident—important but not essential—in the course of the development of the egg from its earliest beginnings up to the finished form.

With respect to segmentation also, there is a broad difference between the two classes of eggs, for segmentation is

generally determinate in mosaic eggs, having a close relation to the already established promorphology of the egg, while in regulative eggs this relation is much looser, or even non-existent. The frog's egg is very definitely transitional between the two. Considering the facts as a whole, we see one point emerge clearly—that there is no necessary connexion between segmentation and differentiation. From a theoretical point of view, the two things are quite distinct. The two processes may in certain cases coincide and reinforce each other, as in the determinate cleavage of mosaic eggs, but this fact cannot be generalized. Both in the mosaic and the regulative egg, segmentation is in reality nothing more than a fragmentation of the substance of the egg; what each blastomere contains depends entirely on its position in relation to the initial structure of the egg as a whole. As Brachet puts it, the fate of each blastomere is determined by the quality and the quantity of the materials which it contains, by those materials which have fallen to its lot as a consequence of the particular mode of segmentation of the fertilized egg (p. 269). Segmentation adds nothing to the original diversity of the egg, though it may help towards further differentiation by segregating specific substances from one another. The egg after fertilization

'is a mosaic of potentialities which have their seat and substratum in the germinal localisations. At the beginning of its development, the egg, in segmenting, divides up into cells (blastomeres) which become progressively smaller and more numerous. So long as no notable displacement occurs of the blastomeres formed, one must consider segmentation as equivalent to a simple division (*découpage*), and each blastomere, in virtue of the germinal localisations of the egg, has its destiny fixed for it by its individual composition. Experiment proves . . . that this dividing up of the egg may take place in quite a different manner from that demanded by the normal laws of segmentation, without the final result of development being altered' (Brachet, p. 192).

The reference in the last sentence is to the well-known experiments on the eggs of sea-urchins and the worm *Nereis*, in which by means of pressure the normal course of cleavage

is upset, without affecting the normality of the result.[1] In sum:

'Segmentation . . . is purely and simply a fragmentation (*morcellement*) of the egg, and has by itself no formative value whatsoever. It creates no new germinal localisations, it does not shift those that exist, and it does not interfere with the bilaterally symmetrical organisation of the egg. The only new fact that appears during its course is that the regional potentialities, in the measure in which they become progressively isolated in particular blastomeres, become more fixed and more stable, and take on a more and more definite determinative character; the mosaic composition of the egg, which is sometimes difficult to discover at the beginning, becomes more definite and precise as segmentation proceeds' (Brachet, p. 259).

Before going on to consider a point which arises naturally out of the preceding discussion, namely the rationale of segmentation, it is desirable to say something about the 'organ-forming stuffs' which characterize the differentiated regions of the mosaic egg.

It is now recognized that the visible substances—pigment, yolk, and so on—that can be distinguished in the egg may have nothing to do with differentiation, since they may be displaced by moderate centrifuging without interfering with normal development. The initial organized structure of the egg, which dominates all subsequent development, is more probably carried by the ground substance of the egg (the hyaloplasm) and the cortical layer. For, while mere shifting of visible organ-forming substances does not upset normal development, 'by very strong centrifuging different areas of the cytoplasm itself . . . may be dislocated, and in such cases development is never normal; even the cleavage cells are atypical in form and position as well as in contents and each of these different kinds of cytoplasm, if it develops at all, gives rise to its own specific part or organ in the larva wherever it may be located. In this way the most bizarre monsters may be formed, with their different organs out of all proper relation to one another.' (p. 19).[2]

[1] See Wilson, 1925, pp. 1059–62.

[2] E. G. Conklin, 'Problems of Development', *American Naturalist*, lxiii, 1929, pp. 5–36.

From the organismal point of view, the so-called 'organ-forming' substances can of course have no actual formative powers—their sole significance is as visible indices of the fundamental promorphology of the egg which is prior to segmentation and determines the first stages of differentiation. It is this initial organization 'as a whole' that adds point to our contention that the egg is only incidentally a cell, but fundamentally the organism-to-be. The fact that the egg *is* a cell has generally been allowed to obscure the more important fact that it is an organism.

4. We have already in Chapter XI devoted some attention to the process of segmentation, with reference especially to the size-relations of the cells and nuclei concerned. We have seen that the egg is a relatively inert cell, with a large inactive nucleus. During segmentation the nucleus is divided up into smaller and smaller units, so that its surface increases considerably. The total mass of the egg does not materially increase up to the blastula stage, though there may be transformation of yolk into protoplasm, but there is synthesis of chromatin and an increase of total nuclear mass. Owing to the repeated division of the nuclear substance the total surface area of the nuclei increases at a much greater rate than the total nuclear mass. We interpret these facts to mean that the metabolic activity of the egg is much increased and facilitated by this splitting up of the egg-nucleus into smaller units. Segmentation may therefore be regarded as a preliminary to further differentiation—a preparation or provision of metabolic units of the most effective dimensions for the future elaboration of organs and tissues.

A somewhat similar view of the rationale of segmentation is taken by Brachet, who emphasizes the significance of the morula and blastula stages as the terminal points of this preparatory work of the egg. Referring to these stages, he writes:

'Their significance consists especially in the fact that they prepare for subsequent differentiation by enabling the blastomeres to attain the normal cell-size of the species to which they belong. The egg is, in fact, a cell the cytoplasmic body of which is considerably hyper-

trophied; the karyoplasmic ratio is profoundly disturbed, and in order that it may be restored it is necessary that the egg should fragment into smaller and smaller cells. By the blastula stage this result is achieved, and one notes as a matter of fact that although cellular proliferation goes on with great intensity, the size of the cells no longer diminishes in any appreciable degree in the later stages. The size maintains itself at this norm, because from this moment onwards the egg takes up nutriment, either at the expense of substances derived from the exterior or by utilising its deutoplasmic reserves. The blastula then marks the end of a period, a sort of critical stage in the physiology of the embryonic cells. The simple fragmentation by which it arises finishes with it, and gives place to the more complex processes of ontogenetic differentiation' (p. 268).

The morula and the blastula form a whole just as does the egg itself, for they are merely the egg divided up into suitable metabolic units.

'During the subsequent course of development, the gastrula, the larva and the adult organism, notwithstanding the growing complexity of their structure, continue to form a whole, of which the parts, however diversified they may be, remain intimately associated. The small initial differences, of a quantitative rather than a qualitative order, become more pronounced in their effects and that for many reasons, but the correlations which lie at their base persist no less, and become even more accentuated' (p. 305).

That segmentation—the actual splitting up of the egg into blastomeres—has really nothing to do with the early processes of differentiation, but at most merely fixes and renders more definite the pre-existent differentiation of the egg, is shown also by the fact that in many eggs, particularly of the Arthropoda, the fragmentation of the nucleus, preparatory to later differentiation, is achieved without a corresponding division of the substance of the egg. Take for instance the development of the Asellid crustacean *Jaera*, as described by McMurrich.[1] In the egg of this form up to the stage with 32 nuclei every cell is organically united with its neighbours, so that the whole embryo forms a syncytium.

'As stated', writes McMurrich, 'this is a highly important fact,

[1] J. P. McMurrich, 'Cell-Division and Development', *Wood's Holl Biological Lectures for 1894*, Boston, 1895, pp. 125–47.

since we see from it that a separation of the protoplasm into distinct spherules, such as presumably occurs in cases of total segmentation, is not necessary in order that histological differentiation may occur. Indeed, such an idea might have been derived from what we know of forms like the infusoria, in which, notwithstanding the fact that they are unicellular, differentiation of the protoplasm into myophanes, for example, occurs' (pp. 140–1).

Even in eggs which normally show complete segmentation, it is possible by artificial means to suppress cleavage and yet obtain a considerable measure of differentiation. This has been done in certain annelid and molluscan eggs, particularly by Lillie in the egg of the worm *Chaetopterus*.[1] Such unsegmented eggs undergo to a certain extent the differentiations characteristic of the normal embryo and may even give rise to ciliated larvae bearing some resemblance to the normal trochophore. Conklin has recently shown that even in an egg showing such a definite and determinate cleavage-pattern as *Styela* some differentiation may take place even though cleavage is prevented.[2]

'I have recently found', he writes, 'that when cleavage is suppressed but nuclear divisions continue in the fertilised eggs of the ascidian, *Styela partita*, the typical localization of the cytoplasms peculiar to the ectoderm, mesoderm and endoderm, the typical peculiarities of the nuclei in these areas, and even some of the histological differentiations of the tadpole stage and of its metamorphosis, may sometimes appear. However, the localization of these plasmas takes place normally at the time of the first cleavage and is provided for before that event; it is therefore not dependent on cleavage' (pp. 13–14).

5. Not only is the early differentiation independent of cleavage, but it is independent even of nuclear division. That there is no qualitative division of the nucleus in early ontogeny is now firmly established;[3] the process is purely quantitative, and the resulting nuclei are all strictly equivalent.

[1] F. R. Lillie, 'Observations and Experiments concerning the Elementary Phenomena of Embryonic Development in *Chaetopterus*', *Journ. Exper. Zool.* iii, 1906, pp. 153–268.

[2] E. G. Conklin, 'Problems of Development', *American Naturalist*, lxiii, 1929, pp. 5–36.

[3] See Wilson, 1925, pp. 1057–62.

It is unnecessary to detail the evidence for this conclusion, but one particularly striking observation of Spemann's may be adduced. By passing a fine loop round the egg of the newt it is possible to divide it more or less completely in two. This operation can be performed on the fertilized egg in such a way that one half contains the zygote nucleus, while the other half contains none. The nucleated part goes on dividing while the enucleate part remains undivided. When 16 nuclei have been formed one is allowed to enter the non-nucleated part, which then proceeds to divide and may give rise to a normal embryo. In this case 1/16th of the zygote nucleus plus a half of the protoplasm still contain all the elements for the formation of a normal embryo, and the system is capable of differentiating itself correctly (p. 187). This result is obtained only if the division of the egg has been into right and left halves; if the constriction is frontal 1/8th of the original nucleus is necessary to bring about development in the dorsal half.[1] The experiment demonstrates clearly that 1/8th or 1/16th of the original nucleus differs from it only in size.

A quantitative nuclear division is found universally in the earliest development of all Metazoa, and we have seen what its probable physiological significance is. It might be expected that if nuclear division were prevented development would be rendered difficult or impossible, owing to the disturbance of the normal surface relations of the nuclei with the cytoplasm. Nevertheless, there is at least one case definitely known where embryonic development can go on (to a certain extent only, and in a somewhat abnormal way), while the nucleus remains undivided, increasing in bulk and in number of chromosomes, but not splitting up into daughter nuclei. This is the case of *Chaetopterus*, fully investigated by F. R. Lillie.[2] By treatment with potassium chloride not only cleavage but even nuclear division can be inhibited in the eggs of this form. Differentiation however goes on, though slowly; the characteristic distribution of substances in the

[1] H. Spemann, 'Vererbung und Entwicklungsmechanik', *Zts. indukt. Abstammungslehre*, xxxiii, 1924, pp. 272–93.
[2] Op. cit., 1906.

egg takes place, and the ectoplasm grows over the endoplasm to form a 'unicellular gastrula'. The embryo develops cilia and swims actively about, and in some cases closely resembles the normal trochophore. Lillie summarizes the results of the differentiation of the uninucleate egg as follows:

'(1) Organs are never formed, but only such structural elements as may occur in single cells of the trochophore. (2) Organs may, however, be simulated by the aggregation of the characteristic matter of an organ, for instance in the case of the yellow endoplasm, which simulates the gut of the trochophore, or the row of large vacuoles situated near the upper margin of the yellow endoplasm which simulates the row of vacuoles of the prototroch. (3) The structural elements appear in the same order of time as in the trochophore. (4) The distribution of structural elements tends to resemble that of the trochophore. (5) The yellow endoplasm (yolk?) is used up, apparently for the maintenance of metabolism, in the ciliated unsegmented eggs precisely as in the larva. (6) The apical flagellum is never formed' (p. 237).

The case is a very important one, for it establishes clearly the possibility of a considerable amount of embryonal differentiation without either nuclear or cytoplasmic division. 'This in itself', Lillie points out, 'is a fact of considerable importance, for it disposes effectually of all theories of development that make the process of cell-division the primary factor of embryonal differentiation, whether in the form of Weismann's qualitative nuclear division, or of Hertwig's cellular interaction theory' (p. 245).

6. Summing up the results of our discussion regarding the early stages of embryonic development, we may conclude that the egg is essentially the organism-to-be, and only incidentally a cell. Differentiation is to be looked upon as not essentially a cellular phenomenon at all, but as a series of events affecting the whole protoplasmic mass of the egg and the embryo. Development is then primarily an activity or function of the organism as a whole, and this is manifest even at the very beginning when the organism is monoenergid. Cell-division and even nuclear division are, strictly speaking, secondary phenomena, and do not in the early stages of

development bring about differentiation, though they may facilitate the course of differentiation and consolidate its progress. The main function of nuclear division during segmentation is to break up the substance of the large inert egg-nucleus and distribute throughout the substance of the egg numerous smaller and more active energid-centres. The nucleus has nothing more and nothing less to do with development and differentiation than it has to do with the other physiological activities of the organism. Being essential for constructive metabolism and the maintenance of life, it is necessarily associated intimately with the processes of development, which could not take place without it. The presence and activity of nuclear substance is then a primary condition of embryonic development, as it is a primary condition of life at all. As Brachet says, with regard to the nucleus,

'It is, in the egg as elsewhere, an essential element of cellular life. If the egg is a cell, it is because it has a nucleus. The nucleus participates in the activity of which the egg is the seat, an activity which after long detours results in the formation of a new organism, and from which nuclear action cannot be excluded; but we do not know in what exactly this action consists, nor exactly what rôle the nucleus plays in the functioning of any cell' (p. 304).

7. In conclusion, a few remarks upon the relation between growth, differentiation, and cell-division in plants may not be without interest, as reinforcing our contention that differentiation is essentially an activity of the organism rather than a composite function of its cellular constituents.

Rauber remarked in 1883 that while most zoologists of his day, following Schwann and Virchow, accepted the elementalist conception of the living thing, and considered differentiation to be the result of cell-activities, the botanists—particularly Hofmeister, Sachs, De Bary, and Goebel—took the opposite view that growth and differentiation were functions of the organism as a whole and cell-division a result rather than a cause of these activities. Rauber himself was on the botanists' side; he pointed out that it is more rational to consider growth as the cause of cell-division rather

than the other way about (p. 252). Sachs devotes much attention to this important question in his lectures on plant physiology.[1] He regards as 'utterly mistaken' the view that growth and differentiation can be ascribed to the activities of individual cells.

'Growth—i.e. the increase in volume and change of form—may take place in plants even without accompanying cell-divisions. In this connection I have already repeatedly referred to the non-cellular plants, such as *Botrydium*, *Caulerpa*, *Vaucheria*, etc., and particularly to the Myxomycetes. It is important to bear this fact in mind; because it proves that the formation of cells is a phenomenon subordinate to, and independent of, growth. The excessive importance for organic life hitherto ascribed to cell-formation found expression in this direction also, in that it was believed that growth depended upon the formation of cells. This is, however, not the case. On the other hand, however, the fact is of course important, that while a few hundred simple forms of plants exist in which growth is not accompanied by cell-division, in all other plants growth and cell-division are intimately connected with one another. In attempting, then, to make clear the relations of the two processes—growth and cell-division—it is above all to be insisted upon that growth is the primary, and cell-division the secondary and independent phenomenon' (p. 431).

It should be noted that Sachs uses the word 'growth' to include differentiation. He regards cell-division as merely a diminution in the size of the chambers into which the living-plant substance is divided, consequent upon growth and conditioned by growth (p. 95). The general plan of growth is determined by the 'growing point' as a whole; what is formed is then secondarily divided up into cells. In the growing shoot of the sea-weed *Stypocaulon*, for example, the shape of the branches and the method of branching appear first, and cell-division sets in only when growth has been completed. We have, in this case, at the upper end of shoot growth without cell-division, and in the older portions of the shoot cell-division without growth (p. 435).

Both in cellular and in non-cellular plants the nuclei are most numerous and most closely crowded together at the

[1] J. von Sachs, *Lectures on the Physiology of Plants*, Eng. Trans., Oxford, 1887.

growing points, from which differentiation sets out; Sachs interprets this phenomenon physiologically, in terms of his energid theory—multiplication of nuclei at these points is necessary to supply the metabolic energy for growth; partitioning off of the energids is a secondary and derivative process.

XIV

THE ORGANISM AS A WHOLE IN DEVELOPMENT AND REPRODUCTION

'THE point of departure for every approach to the problems of inheritance and development is given by the fact that the germ is originally a single cell, equivalent in all of its essential features to any one of the tissue-cells of which the body is composed.' This dictum of Wilson's[1] well represents the current state of opinion as to the proper method of interpreting heredity and development. It is generally held that these are essentially cellular phenomena, and that the clue to their understanding is to be found in the study of the cell and of the constituents of the cell. Every organism begins life as a single cell; development is brought about by the multiplication of this original egg-cell, and by the subsequent interaction and differentiation of the multitude of cells so formed. From this point of view the proximate task of developmental physiology is to analyse the processes of development in terms of cell-activities, the cell being regarded as the fundamental morphological and physiological unit.

We have seen in the last three chapters that the cellular view of development requires correction and modification. It expresses only part of the truth. Its method is abstract and analytical, and it leaves out of account the fundamental truth that the developing egg is from the very beginning a unitary organism—at first monoenergid, later polyenergid. This primary unity of the developing organism the cellular theory ignores. We have seen (Chap. IX) that the method of analytical abstraction resolves the organism into a coordinated assemblage of parts, and invests the parts so distinguished with a certain independence and separateness which they do not in reality possess. From these conceptualized 'parts' it is, we have seen, impossible fully to recon-

[1] 1925, p. 980.

stitute the original unity from which they have been derived by abstraction. The whole cannot be completely explained from the parts into which conceptual analysis resolves it; the unity of the developing organism is therefore not explained on the cellular view, which has the inherent faults of the uncorrected analytic method.

Quite apart from these theoretical considerations, the facts of development clearly show that the germ is primarily an organism, and only incidentally a cell. The evidence is conclusive that segmentation and differentiation are two distinct processes; cell-formation often facilitates differentiation, but differentiation may go on quite independently of it. The egg as a whole, whether in its monoenergid or its polyenergid form, shows a primary differentiation *as organism*, and this is independent of the degree to which it is subdivided by the process of segmentation. In respect of this primary organismal differentiation the polyenergid blastula is approximately the equivalent of the fertilized monoenergid ovum.

We have further seen that the formation of discrete cells is not a universal phenomenon in the organic realm. Early development may be syncytial, and adult organisms that are polyenergid but unicellular are known. Hence multiplication of nuclei is a more general phenomenon than multiplication of cells, and a 'nuclear' theory is of wider application than a cell-theory. We have been able, following Sachs, to suggest a reason for the multiplication of nuclei and their dispersal throughout the body—it is because they are necessary for all processes of constructive metabolism, particularly of growth and repair. They can apparently act effectively only if their surface is large in proportion to their volume, that is, given their spherical form, if their absolute size is small; they cannot function save in continuity with the cytoplasm, and as a rule their sphere of influence is strictly limited spatially. On the energid theory the developing and adult organism must be regarded as essentially a protoplasmic whole, just as it is in the egg-stage. The number of energids necessary to maintain the vital metabolic activities is in the main a

function of the size of the organism—large organisms are necessarily polyenergid, small organisms may be mono-energid. It is irrelevant to the energid conception whether the cells of the organism are spatially distinct from one another or not. Cell-formation is something superadded to multiplication of nuclei; it has an important function to perform in facilitating differentiation—no very high degree of organization is reached by non-cellular organisms, even when their nuclei are numbered in thousands—but it still remains something secondary.

For all these reasons it seems clear that for the cellular theory of development, which contains no more than a part of the truth and that expressed abstractly, there must be substituted an organismal conception, which shall take account of those broader characteristics of development with which the cellular theory is powerless to deal. We have already gathered the first fruits of the organismal method in that it has shown us the inadequacy of the cellular theory of development.

2. If the cellular conception of development fails by reason of ignoring the essential unity of the organism from the egg-cell onwards, how much more does the nuclear or chromosomal theory fall short of completeness and adequacy. If development is not primarily a matter of cells and their activities, it is still less a matter of the chromosomes and their presumed organizatory powers.

We have in previous chapters outlined our general criticism of the germ-plasm theory, the gene theory, and the underlying conception of nuclear dominance and control. Into detailed criticism of the special theories we need not enter again, but it is desirable to consider once more the general chromosome theory, to discuss what its shortcomings are, and also to utilize what amount of positive truth it contains in the building up of a more adequate, less abstract, conception of development and heredity.

According to the chromosome theory there is contained in the nucleus an organized structure, built up of discrete self-perpetuating units, which constitutes the material basis of

heredity and is the main determining cause of development. Suitable general environmental conditions are admittedly necessary for development, and particular conditions may be essential for the appearance of particular characters—duplicity of legs, for example, in *Drosophila* is dependent not only upon a 'mutant gene' but upon low temperature. But in general the environment does not account in any way for the specificity of development—this is entirely due to the nuclear or genic organization. Even the cytoplasm, according to the theory of nuclear dominance, plays a very minor role in the essential determination of development; Morgan roundly asserts that '... except for the rare cases of plastid inheritance, the inheritance of all known characters can be sufficiently accounted for by the presence of genes in the chromosomes. In a word, the cytoplasm may be ignored genetically'.[1] We may recall in this connexion the dictum of McClung that the chromosomes represent the sum total of the elements of control over vital processes (see above, p. 154).

If inheritance is thus determined by the chromosomes alone, it follows that the course of development is also so determined, for inheritance is merely an expression for similarity or quasi-identity of developmental process.

As a moderate and judicial statement of the chromosome theory let us take the following passage from Wilson:[2] 'All the available evidence indicates that the nucleus is indeed a kind of "original preformation" in which are contained great numbers of self-perpetuating, definite entities grouped in a definite though shifting pattern. Their nature is unknown. They are conceivably single molecules of nucleoproteins, in which the protein complex may perhaps be the determining element to which the different genes owe their several specific characters. Heredity may thus be determined fundamentally by the chemical constitution of the various proteins.' It is, however, more probable, Wilson considers, that the heredity units are molecular aggregates which multiply by division. Even when characters appear to be

[1] T. H. Morgan, 'Genetics and the Physiology of Development', *American Naturalist*, lx, 1926, p. 491.
[2] 1925, p. 1111.

preformed in the cytoplasm, as in germinal pre-localization, the most likely explanation is that they have been formed under the influence of the chromosomes. It would in Wilson's opinion be 'highly misleading to state that the "embryo in the rough" is determined solely by the cytoplasm. The cytoplasmic characters of the ovum are themselves the product of biparental heredity, even though they may be determined before the sperm enters' (p. 1108). Wilson's matured and reasoned view is 'that in respect to a great number of characters *heredity is effected by the transmission of a nuclear preformation which in the course of development finds expression in a process of cytoplasmic epigenesis*' (p. 1112).

These quotations from Wilson leave no doubt as to the essentials of the chromosome theory. The basis of heredity and the determining factors of development are internal to the organism and internal to its cells. There is a mechanism inside the nucleus to which are due the visible transformation of the organism during development and that stereotyped repetition of the course of development which we call heredity. This theory of an internal and invisible mechanism that dominates and controls the outer manifestations of vital activity is stated with peculiar clearness in a recent paper by Conklin. 'We know', he writes, 'that the organism consists of machines within machines. The inner machine in every cell is the nucleus, usually containing two sets of chromosomes and genes, any one set of which is capable of giving rise to an entire organism if it is not prevented by the outer machine consisting of cytoplasm and the products of differentiation.'[1]

We have earlier on discussed in general terms this theory of an internal mechanism, and noted the curious analogy between the formative germ-plasm and the entelechy of Driesch. In both theories there is evident a dualism of agent and material; the germ-plasm, even in its modern genic form, is something which itself remains unaltered while acting as the cause of visible change in the organism. Aristotle

[1] E. G. Conklin, 'Problems of Development', *American Naturalist*, lxiii, 1929, p. 30.

would have recognized in this almost mystical conception something strangely like his 'soul'! We cannot however enter farther into the curious methodological and psychological problems here involved. We are concerned primarily with the validity and adequacy of the chromosome theory of development and heredity as an explanation of these phenomena, and we must pass on to consider the evidence on which it is based, and the logical processes by means of which it has been built up.

3. The strongest point in favour of the chromosome theory has been the fact that in fertilization there is a union of exactly equivalent male and female pronuclei. This is the essential thing in normal fertilization. The egg and the sperm may be utterly different in size and in structure, yet they are exactly equivalent in respect of their nuclei. It appears on the face of it obvious that the paternal and the maternal contributions to the hereditary equipment of the offspring are approximately equal. Hence, it is argued, each contribution must be carried by the only exactly equivalent structures in the gametes, namely the chromosomes. Hence the chromosomes represent the 'material basis of heredity'.

In illustration of this usual train of reasoning let us take a passage from each of two recent and well-known text-books of cytology. The first from Doncaster:[1]

'we know that in general the father and mother contribute equally to the hereditary features of their children, and yet in Man the whole of this almost infinitely complex web of family likeness is transmitted, on the father's side, by a spermatozoon about one five-hundredth of an inch in length' (p. 207).

The second, more elaborate, from Agar:[2]

'The fact that, on the average, offspring inherit with approximately equal intensity from both parents, whereas the macrogamete as a whole is nearly always enormously larger (often a million or even more than a billion times larger) than the microgamete, immediately suggests that the hereditary substratum is not the substance of the

[1] L. Doncaster, *Cytology*, Cambridge, 1920,

[2] W. E. Agar, *Cytology with Special Reference to the Mammalian Nucleus*, London, 1920.

gametes as a whole, but some special portion of them which is of more approximately equal mass in the two cells. This consideration led Nägeli in 1884 to postulate two substances in the gametes, one of which is present in equal amount in the micro- and macro-gamete. This is the bearer of hereditary qualities—the *idioplasm*. The other has mainly a nutritive function and is present in far greater amount in the egg and is indeed responsible for its larger size. Knowledge of the processes of fertilization naturally led to the idioplasm being identified with the nucleus (independently by O. Hertwig and Strasburger in 1884), since the nuclear substance appears to be the only one that is contributed in approximately equal amounts by the two gametes. Mere study of the anatomy of the gametes therefore at once leads us to suspect the all-importance of the nucleus and the essential passivity of the cytoplasm in the transmission of hereditary qualities' (p. 154).[1]

We have already exposed the weak spot of this commonly accepted argument (see above, p. 68), which lies in the fact that it is quite impossible to prove that the maternal and paternal contributions are in fact equal, that the offspring inherits from both sides a *full* complement of hereditary potentialities. When we say that a child shows a hereditary likeness to its father, we mean that it resembles its father more closely than it does the average of the population. The likeness is observable in respect of those individual characteristics that distinguish the father from the rest of his race. If the child shows no particular resemblance to its father, but takes after its mother, we say that it has inherited specific hereditary traits from the mother—those traits or some of them that distinguish the mother as an individual from other individuals of the same race. If by exception the child showed no particular resemblance to either of its parents we should then say that there was no specific paternal or maternal inheritance at all. But yet in all three cases the child would show the characteristics of its species and its race—it would be a human child, distinguishable as belonging to the same racial type as its parents.

This general resemblance in type may then be distinguished

[1] This passage is interesting also as showing how essentially morphological and abstract is the separation of nucleus and cytoplasm.

from the special resemblance to one or both of the parents, or to more remote ancestors of the direct line. It is these *special* resemblances and differences that have been the subject of the modern study of heredity, whether by biometrical or by genetical methods. The broad general resemblances of type give no hold for experimental or statistical treatment, and have accordingly on the whole been ignored. But it is this *general* hereditary resemblance which constitutes the main problem.

We saw in discussing the gene theory that it deals only with *differences* between closely allied forms, and with the modes of inheritance of these differences; it leaves the main problem quite untouched as to why, for example, from a pair of *Drosophila* only *Drosophila* arise. It takes for granted the inheritance of Johannsen's 'great central something'—the general hereditary equipment of the species.

Now there is no means of telling, even by breeding experiments, whether the general hereditary equipment comes from one parent only or from both. In intra-specific crosses all the main characters, those of the phylum, the class, the order, the genus, and the species, are common to both parents; what characters in the offspring can be definitely ascribed to one or other parent can only be those that distinguish one parent from the other, characters therefore of less than specific rank. In inter-specific crosses the differences may be larger, and the respective contributions may thus be more readily distinguishable, but even here the overwhelming majority of important characters are common to both parents. The fact that true crosses between quite diverse types are impossible to realize imposes of course a strict limit on this mode of analysis.

To put the matter in another way—if in a normal cross the maternal and paternal contributions were equivalent, they would be almost identical, that is to say, they would have almost everything of importance in common. It would be possible then to relate a character in the offspring to the maternal or the paternal side only if this character were different in the male and the female parent. Such differences

could by the nature of things be only minor differences—either differences in minor characters, or minor differences in major characters. *Exactly the same result in crossing would be obtained if the main hereditary potentialities came from one parent only, and the other parent merely modified in its own direction the fundamental hereditary constitution.* It is therefore impossible to be certain that the main hereditary equipment comes from *both* parents—it might equally well come from one only, and that of course, from other evidence, the female.

The 'axiom' that the maternal and paternal contributions are equal is therefore no axiom at all, but a begging of the question, and the argument from this supposed axiom falls to the ground. The correctness of the chromosome theory is therefore not logically established by this line of argument, and the question as to the material basis of heredity (if there be such a thing) remains completely open.

Though most authors have accepted uncritically this faulty chain of reasoning, one or two have realized its lack of cogency, notably Winkler.[1] Regarding the supposed equivalence of the paternal and maternal contributions in heredity, Winkler writes:

'The union of nuclei is only part of the process of fertilization, and its closer fathoming, in all those cases where pure isogamy is not found, has led to the recognition of the fact that the two parents contribute quite unequally, both as regards amount and as regards quality, to the formation of the cell which is the origin of the new individual. It would certainly be natural to conclude from this that the two parents were unequally concerned in the transmission of the genotype. If the opposite conclusion is commonly drawn, this is by reason of the *petitio principii* that both parents are concerned in heredity in approximately equal measure. As proof of this there is advanced the intermediate character of many hybrids. But obviously this merely shows that both parents take part in general to an equal degree in the transmission of those characters in which they *differ* from one another. The behaviour of hybrids however can shed no light upon the question as to how and by what means there is brought

[1] H. Winkler, 'Ueber die Rolle von Kern und Protoplasma bei der Vererbung', *Zts. indukt. Abstammungslehre*, xxxiii, 1924, pp. 238–53.

about the reappearance in the offspring of all those characters in respect of which the parents are *alike*. It is possible that both parents are equally concerned in the appearance of these characters also; but it is equally possible that the primordia for the development of these characters are transmitted by one parent only' (p. 239).

Winkler concludes from this that the common 'proof' that the hereditary characters are borne exclusively by the chromosomes lacks solid foundation. He himself considers that the cytoplasm must contain the genes responsible for *general* as distinct from *special* heredity. These cytoplasmic genes form a homozygous 'Grundstock', which is answerable for the appearance of the more important and fundamental characters of the organism. The nuclear genes have to do only with the transmission of relatively unimportant and superficial peculiarities, such as obey the Mendelian laws.

It follows from this way of looking at things that

'the two kinds of gametes are not of equal significance for heredity, but to a high degree unequal, inasmuch as an important part of the genotype is transmitted only by the female germ-cell. . . . And if we ascribe to the female germ-cell so much greater importance for the transmission of heritable characters than to the male germ-cell, this does not mean that a greater effect is exercised by the mother than by the father on the genotypical *particularity* of the offspring. For what the mother alone transmits to the child consists only of those things in which she is identical with the father; it is just the continuity of cytoplasm solely in the female line that brings about complete identity of the cytoplasms in all descendants, whether they are of the male sex or the female. Even if the father contributed on his side cytoplasm to the constitution of the zygote, he could only transmit approximately the same characters as the mother. And that would be superfluous' (p. 252).

4. We can take this fundamental question of the equivalence or non-equivalence of the gametes a stage farther by considering the point of view developed by Brachet.[1] He draws the same distinction as we have done above between general resemblance and special resemblance.

'In the development of every individual', he writes, 'two distinct groups of hereditary tendencies are concerned; the first constitute

[1] A. Brachet, *L'Œuf et les Facteurs de l'Ontogénèse*, Paris, 1917.

together *general heredity*, the second may be united under the name *special*, or more properly, *personal*, *heredity*. . . . General heredity is the totality of the causes, factors and laws, thanks to which a fertilised egg gives rise to an individual of the species to which it belongs. Its composition, the wheels of its mechanism, limit the egg to two possibilities only—regular development or death.[1] The egg possesses this essential part of the hereditary patrimony, this capability of building up a new organism according to definite laws, but all the facts so far known unite to prove that the spermatozoon is devoid of this power. . . . As for special heredity, it comprises that which, in each individual egg, is added on to general heredity; it is that which gives the "personal turn" to heredity, if one may use the expression. This it is which gives to the development of each individual, or rather of all the individuals born of the same parents, a particular impress, sometimes easy to discover, sometimes on the contrary indistinct and obscure. General heredity and special heredity are never superimposed; there is never any clash between them, and the latter is in effect only a special case of the former. Accordingly it is incorrect to limit, as some have done, the action of general heredity to the first phases only of development, conceiving that it yields place progressively to special heredity; the latter impresses its personal seal from the beginning, provoking differences, minimal it is true, but none the less real. . . . These premisses being agreed, it is easy to conceive that in the development of a fertilised egg, the *heredity contribution of the spermatozoon affects only the special side of heredity*' (pp. 176–8).

The egg is, as we have seen, demonstrably the organism-to-be, the new organism in its simplest, monoenergid state; it is so, not in respect of its chromosomal constitution, but *as a whole*, as a functioning nucleo-cytoplasmic system. We know further, from the numerous examples of natural and artificial parthenogenesis which observation and experiment have revealed, that the egg contains within itself the full potentialities of development, and can in fact develop to a fully adult stage without the help of the spermatozoon. The case is quite different with the spermatozoon. It *cannot* develop into a new organism, in spite of the fact that on the chromosomal theory it possesses all the necessary genes. All

[1] Cf. Delage, p. 80 above. There is much similarity of thought between Delage and Brachet.

the experiments made to induce spermatozoa to develop their own potentialities in a suitable cytoplasmic medium have failed. We have no right then to assume that the spermatozoon does in fact possess the complete hereditary equipment of the species; the plain facts teach otherwise, and it is only theoretical and poorly based considerations that would persuade us otherwise.

It is doubtful even whether the spermatozoon can properly be called a cell, for it is probably incapable of constructive metabolism, growth or division; it can certainly not rank as an organism, for it cannot maintain itself for any length of time as an active unity; it is merely a mechanism for transporting a nucleus. The egg and the sperm are therefore, as plain observation shows us, completely unlike—as unlike as two 'cells' can possibly be. The only equivalence is between the nucleus of the sperm and the nucleus of the egg. In fertilization the nucleus of the sperm is added to and becomes an integral part of the nucleus of the ovum. The ovum is not by this process essentially changed; it remains the organism-to-be, with perhaps some re-arrangement of its cytoplasm as the first step in development (and this start in development can be brought about by other means than the entrance of the sperm); it may be modified as regards its special heredity by the introduction of the male chromatin, but there is no reason to assume, having regard to the similarity between parthenogenetic and sexual development, that its general hereditary potentialities are seriously altered, or added to.

This is the general view of the relative importance of egg and sperm which we are led to adopt if we regard only the facts and eschew the theoretical interpretation offered by the germ-plasm theory. It is in general outline the view adopted by Brachet, with the sole difference that he prefers to think of the egg as a cell—the 'type-cell' of the species—rather than as a monoenergid organism. Brachet lays much stress on the fact, which we have already indicated, that in respect of their developmental potentialities the sperm and the ovum are totally dissimilar. His argument is as follows. If we place the sperm in a suitable nutritive medium, for example

an extract of crushed eggs of the same species, as has been done by De Meyer, we do not find that it can assimilate and organize this material into an egg nor initiate any developmental process. At most the sperm head swells up and forms a sort of pronucleus. Again, experiments on intra-specific merogony merely show that the male pronucleus is the exact equivalent of the female pronucleus, and can replace it in development. Giard has attempted to regard merogonic development as a case of male parthenogenesis, but this possibility is negatived by the results of merogonic crosses between animals belonging to different families, and by the facts of polyspermic development in Anura. In the well-known experiments of Godlewski, in which an enucleate fragment of an *Echinus* egg was fertilized by *Antedon* sperm, the early development is purely maternal; the sperm remains inactive and exercises no influence on development. It is clear from such cases that the cytoplasm of the egg is much more than a nutritive medium for the nucleus, for it determines by its own powers [1] the early course of development.

The case of polyspermy in Anura is even more demonstrative. Under certain conditions, as when sperm are supplied in high concentration, the egg of *Rana* can be penetrated by a considerable number of spermatozoa at once. The sperm heads turn into typical pronuclei; one of them unites with the pronucleus of the egg, while the others, scattered throughout the substance of the egg, develop asters and divide up the egg between them into so many zones of influence, forming as many 'spermatic energids' as there are male pronuclei present. Now when development starts, all the nuclei of the polyspermic egg enter simultaneously into typical bipolar mitosis. Each male pronucleus acts exactly like the nucleus of a segmentation cell, *and the egg segments and develops as a whole.* If the spermatozoon were really totipotent, if it imposed on the surrounding cytoplasm a development determined by its own powers, each energid would act on its own, and the development of the egg as a whole would be quite chaotic. On the contrary, in successful

[1] Provided some sort of nucleus is present, or at least nuclear matter.

cases, perfectly normal larvae are obtained, capable of hatching and living for several days (p. 125). If each sperm nucleus really contained the potentialities of complete development, we should expect each to initiate the formation of an embryo; instead of which each fits in with the others and co-operates in the developmental processes of the egg as a whole.

'One essential conclusion emerges from these experiments; it is in contradiction, not only with the idea of Giard, but also with all the theories that maintain the potential equivalence of the male and female gametes. It may be formulated as follows: the destiny of a spermatozoon, or more generally of a pronucleus or even of any nucleus whatsoever, is absolutely dependent on the quality of the cytoplasm in which it finds itself situated. It is an agent of division, it plays undeniably a rôle in the carrying out of cellular metabolism, and it can even, eventually, impress on the cytoplasm certain characters of minor importance, but that is all. In sum . . . we may say that in the present state of our knowledge the spermatozoon of the Metazoa possesses neither virtually, nor even in a latent state, the potentialities necessary for the formation of an organism similar to that from which it is itself derived. Experiment has so far proved the correctness of this notion, whose biological significance is considerable; the objections that may be raised to it, if they have no other basis than à priori reasoning, cannot upset it' (pp. 126–7).

While the spermatozoon by itself is quite incapable of development, the case is quite different with the egg. Experiment clearly proves that the egg has no need of any contribution from the sperm in order to develop normally. We can safely deduce that the potentialities of the egg differ fundamentally from those of the spermatozoon, that the egg is really totipotent, and that the union of the two pronuclei, with the consequent re-establishment of the normal number of chromosomes, is not a condition *sine qua non* of the development of the egg (p. 131).

5. It may be well here to refer to the famous experiments of Boveri (1889) on the fertilization of enucleate fragments of *Sphaerechinus* eggs by the sperm of *Parechinus* or *Paracentrotus*. The original experiments appeared to show that the resulting pluteus larva might exhibit purely paternal

characters, and this result was hailed as affording conclusive proof of the primacy of the nucleus in the determination of hereditary characters. Boveri however at a later date submitted his original conclusions to very close and critical scrutiny; he went to immense pains to repeat his experiments on an adequate scale, tracking down every possible source of error. In a remarkable paper [1] published after his death, he came to the conclusion that his original experiments were faulty, and that no definite proof existed of the determining influence on larval characters of the paternal chromatin introduced into the enucleate egg. He showed that in the original experiments the egg fragments that gave rise to plutei were almost certainly nucleate, or at least contained a portion of the egg-nucleus. Real merogony he found to be possible between *Parechinus* ♀ and *Paracentrotus* ♂, but the larval characters in the two forms are so similar that no deduction could be drawn as to the influence of the male pronucleus. Elaborate tests of the original merogonic cross *Sphaerechinus* ♀ × *Parechinus* or *Paracentrotus* ♂ gave the following simple and definite result:

'Judged by the criterion of nuclear size, the enucleate fragments of *Sphaerechinus* eggs after fertilisation with *Paracentrotus* or *Parechinus* sperm develope at first equally well with the nucleate fragments. After the completion of the blastula stage, however, they do not keep pace with these, and soon cease to develope. The furthest developed that we found in the three cultures had stopped short during gastrulation. Two tiny three-pointed stars were the most they produced in the way of a skeleton' (p. 441).

Thus instead of the well-developed plutei, so often figured as the result of the merogonic cross, the real products of the fertilization of an enucleate fragment by foreign sperm were little aborted larvae which did not get beyond the gastrula stage. In his general conclusions Boveri draws attention to the fact that 'certain very general form-relations of the developing individual are undoubtedly predelineated in the

[1] Th. Boveri, 'Zwei Fehlerquellen bei Merogonieversuchen und die Entwicklungsfähigkeit merogonischer und partiellmerogonischer Seeigelbastarde', *Arch. f. Ent.-Mech.* xliv, 1918, pp. 417–71.

arrangement of the egg-cytoplasm. We recognize in eggs of various groups more or less detailed plasmatic differentiations, by which the axis of the embryo, the point of gastrulation, and of the appearance of other primitive organs is already marked out' (p. 465). It would appear, Boveri considers, from the results of his experiments, that *any* chromosomal equipment is good enough for the earliest development of the embryo, up to the beginning of gastrulation. But thereafter chromosomes of the same species, or of a closely allied species (as in the *Parechinus* × *Paracentrotus* merogonic crosses) are required for further development. Thus 'with *Sphaerechinus* protoplasm the *Paracentrotus* nucleus cannot carry development beyond that first period in which we may consider formative relations between nucleus and cytoplasm to be absent. If then we mean by heredity the totality of the internal conditions which relate to the unfolding of the characters of the new individual, a much more specialized importance attaches to the protoplasm than most people have hitherto been willing to suppose, and the opinion that it should be possible to induce a sperm to develop in an artificial culture medium appears more absurd than ever' (p. 466).

Though Boveri still adhered to the view that the nuclear substance constitutes the material basis of heredity, he admitted that the cytoplasm might play a considerable part, and he also indicated the possibility that the nucleus might be regarded as being merely a 'factor of development' and not the sole bearer of the hereditary equipment (p. 467).

It is of methodological interest to note that Boveri considered the 'Grundfrage' or fundamental question at issue to be whether the egg-cytoplasm without its own nucleus could develop specific maternal characters. This, however, as we saw in Chapter IX, is not the correct formulation of the problem. Nucleus and cytoplasm *considered in isolation from each other* are abstract notions; the only real self-existent thing is the cell or cell-organism. There is clearly a danger in attempting to separate and contrast too absolutely the respective parts played by nucleus and cytoplasm in heredity

and development. A false antithesis of nucleus and cytoplasm is thus set up, and their natural unity as an organic system destroyed. As we have seen, the true formulation consists in regarding the egg as the organism in its earliest form, possessing *as a whole* the full potentialities of development. If for the pronucleus of the egg there is substituted a male pronucleus of the same species, development goes on normally, because the original nucleo-plasmatic system or individual is reconstituted approximately as it was. If a pronucleus which is too different is substituted, development proceeds only a little way, presumably because the foreign chromatin cannot settle down with the egg-cytoplasm, and co-operate with it in metabolism and development. Actually the complete egg is the organism-to-be, and the sperm nucleus is merely a possible *modifier* of development, a factor conditioning its course. The sperm is then in no sense the equivalent of the egg; it is the equivalent merely of the egg-nucleus. There is no proof whatsoever that it contributes to the egg a complete set of hereditary potentialities; the evidence in fact all points the other way.

6. We can now formulate a working hypothesis of the part played by the chromosomes in heredity and development. We have seen that they are not to be regarded as the sole bearers of the hereditary potentialities. The evidence indicates clearly that they are to be considered as *conditioning factors* of heredity and development, not as fully determinative effectors of these processes.

It will be remembered that in Chapter X we discussed in general terms the relations between the organism, the cell, and the subordinate parts of the cell. We saw that the action of the whole could not be fully accounted for by the actions of the parts—that for example the activity of the organism as a whole was not a mere summation of the activities of its cells. The cell-activities condition and implement the action of the whole, but they are not independent elements from which the action of the whole can be derived by addition. The unity of the whole has been destroyed by the very fact of distinguishing separate, semi-independent parts or centres

of activity, which have no real existence apart from their relations with the whole, and it cannot be reconstituted by summation of these abstract parts. The method of analytical abstraction introduces in fact discontinuities and separatenesses which do not exist in nature; the tissue cell, for instance, considered as an independent centre of activity, apart from its relations to the whole, is to a very large extent a fiction or conventional abstraction.

We distinguished in general the *modes of action* of higher and lower unities—from the mode of action of the organism as a whole down to the modes of action of those parts of the cell which, like the chromosomes, show a certain measure of independence and individuality. We came to the conclusion that the modes of action of the subordinate unities condition, both in a positive and a negative sense, the modes of action of the higher unities. Being integrated into the activity of the whole they render possible the vital manifestations of the whole, and at the same time they limit the mode of manifestation of these activities by imposing on them a particular form.

It is along these lines that we must interpret the nature and activities of the chromosomes. They are semi-independent units, possibly genetically continuous from one cell-generation to another, if the theory of the individuality of the chromosomes is to be believed. They have obviously an important role to play in cell-metabolism; they appear to be absolutely indispensable for all processes affecting the growth and repair of the cell; and it is highly probable that they exercise a profound influence on the general metabolism of the organism. Their exact physiological functions are not known with any certainty, but the classical experiments with enucleated Protozoan cells appear to indicate that the nucleus is the main source of the enzymes concerned in constructive metabolism. Some of the Mendelian results, especially as regards colour inheritance, also appear to point towards the conclusion that the chromosomes are the centre of production of oxidases and other enzymes. Many authors have in fact looked upon the nucleus as the main producer of enzymes and hormones. 'How genes or chromosomes operate', writes

Wilson, 'is unknown; but we may suspect that they, like plastids and other cytoplasmic bodies, are centres of specific chemical action, and possibly may serve for the production of soluble enzymes or hormones' (1925, p. 1113). However this may be, there can be no doubt that their physiological influence is profound.

The fact that, owing to the exactitude of mitotic division, the chromosome complex is apparently identical in all the cells of the body seems to show that the individual nuclei exercise no direct or *specific* influence upon the differentiation of the cells severally containing them (see above, pp. 70–3). They are necessary for the life and maintenance of the cell, and in this sense they are the most important of the cell-organs, but that they exercise a direct or active modifying or morphogenetic action upon the cytoplasm is both unproved and improbable. Being universally distributed throughout all the living parts of the body, it is more probable that their effect is a massed one, exercised through the *milieu interne* upon the general metabolism of the body.

If then we may assume that the chromosomes as a whole profoundly affect general metabolism, any slight modification of one or more of them may be expected to alter in a definite and specific way most or many of the characters of the organism. This is in fact what we find in Mendelian inheritance. The evidence is fairly clear—quite apart from its interpretation in terms of the gene theory—that the individual chromosomes of a set differ from one another in their effects upon the organism; it is probable even that different parts of the same chromosome are qualitatively different from one another. It is nearly certain that the transmission of Mendelian differences is bound up with, and explicable in terms of, the distribution of particular chromosomes in reduction and fertilization. It is generally agreed by geneticists that the effect of a modification of a chromosome, the effect of a mutant gene, is widespread throughout the organism, affecting to some degree many or most of the characters of the organism, but some much more definitely and visibly than others.

This is all perfectly understandable on the view that the chromosomes normally play an important role in general metabolism, for any slight modification of the chromosomal complex, e.g. the substitution of a mutated chromosome for a normal one in fertilization, is perpetuated throughout all the cells of the body; it is therefore to be expected that the metabolic processes of the organism will be definitely modified as a whole. But because rather definite and specific *differences* between individuals can be tracked down to *differences* between their chromosomes, it does not in the least follow that the chromosomes are the sole determiners of all the characters of the organism. It is clear that the physiological functions of the chromosomes are important for the life, and hence for the development, of the organism. It follows that the characters of the organism are in part determined by the particular modes of metabolism manifested by the particular chromosomal set which is present in all its cells. This comes to light especially clearly when differences between homologous chromosomes arise, and the visible effects of such mutations can be traced by genetic experiment. The chromosomes therefore, being essential elements in general metabolism, clearly take part in the determination of the characters of the organism, but they are not the exclusive determiners; they condition, but they do not *fully* condition (i.e. determine), the appearance of these characters.

In heredity and development the whole nucleo-plasmatic system of the egg is involved; the general hereditary potentialities are the possession of the egg-cell—the monoenergid organism—as a whole. The chromosomes brought in by the sperm merely modify slightly the general potentialities of the egg-cell or egg-organism; they do not duplicate these potentialities nor even transform them profoundly.

If the male chromosomes merely modify development, then the chromosomes of the egg, which experiment shows to be their exact equivalent, must also be regarded as partial determiners, as conditioning factors, not as sufficient causes or full determiners of heredity and development.

The truth of this conclusion, that the chromosomes cannot

by themselves be responsible for development and heredity, may be verified by considering a further implication of the organismal point of view. If the activity of the organism as a whole is not completely reducible to the modes of action of its parts, then it follows that the modes of action of the whole, whether actual or potential, can be transmitted only by a whole, i.e. by the egg in its entirety, which at the very beginning of development *is* the new individual. Subordinate parts of the egg-organism can transmit only their own particular modes of action, and not the modes of action of the whole; they cannot transmit even their own modes save as integral parts of the whole. A plastid, for example, which is transmitted *en bloc* in the plant ovum, carries over only its own capabilities, and these cannot be manifested except in connexion with the whole. In the same way, the chromosomes, considered in isolation, can transmit only their own modes of activity, presumably particular metabolic rhythms, and that only while they remain parts of the whole. Finally, any specific chemical substances that are handed on as such from one generation to another, transmit merely their own chemical characteristics and modes of reaction. There are thus diverse grades or levels at which transmission is possible, but only the whole, which includes all these grades, can transmit the potentialities of the whole.

From the organismal point of view, then, it is impossible that heredity and development should be accounted for by the sole action of the subordinate parts of the egg-cell, for these cannot transmit the potentialities of the whole.

7. The conception which we have reached of the role played by the chromosomes in development and heredity is, as we have seen, consonant with the facts of Mendelian inheritance, though not with the theory of the gene, which is an abstract and morphological rendering of these facts, restating them in terms of hypothetical particles. Instead of trying to separate and distinguish the action of the nucleus in development and heredity from the action of the cytoplasm, according to the analytic method, we have been led, by adopting the synthetic view, to regard nuclei and

cytoplasm as integral parts of one unitary system or organic individual, as being equally concerned in the life and activities of that individual. We do not consider for example, like Conklin and Loeb, that the 'embryo in the rough' is determined by the cytoplasm only, any more than we agree that the chromosomes are solely responsible for the finer characteristics which appear later in development. Nor do we agree with Jenkinson[1] that the cytoplasm determines the broad characters of the organism, those of its phylum, its class, order, and family, while generic, specific, and individual characters are transmitted by the nucleus. For us, nucleus and cytoplasm are indissolubly wedded in their action upon development; the influence of the chromosomes is exerted from the very beginning, so that a mutated chromosome may modify development from the very start.

We have further drawn no hard and fast distinction between the individual in its monoenergid state, as an egg 'cell', and its polyenergid state as an embryo; for us it remains always one and the same organic individual. The polyenergid system which develops from the monoenergid egg we regard as a unitary individual, not as the cell-state or colony, into which the cell-theory would have us resolve it. Nor on our view is the developing organism formed and actuated by a mysterious internal and invisible mechanism concealed in the chromosomes, as the germ-plasm theory would have us believe.

The germ-plasm is indeed a totally superfluous and otiose conception. The facts do not demand it; it arises purely from theoretical considerations, which do not impose themselves, and its main effect is to introduce a maze of complexities and artificial problems into the theoretical interpretation of development and heredity.

The trend of opinion is fortunately away from belief in a fully determinative germ-plasm, and it may be hoped that when the purely fictive nature of the gene is more generally realized the last traces of this scholastic notion will disappear.

[1] J. W. Jenkinson, *Three Lectures on Experimental Embryology*, Oxford, 1917, p. 98.

Describing the historical evolution of the germ-plasm theory, Wilson writes:

'In the light of these discoveries [by Roux and Boveri] and their later development it became evident that the nucleus cannot be thought of as composed of a single, homogeneous idioplasm or germ-plasm. It is a biological *system*, built up from a specifically organized group of different chromosomes which are themselves highly complex bodies; and it is only one part of a larger protoplasmic system, represented by the germ-cell as a whole. The term idioplasm or germ-plasm thus lost much of its original meaning; nevertheless it is often convenient as a collective name for all those components of the cell-system, whether nuclear or cytoplasmic, that are transmitted from generation to generation and which embody the primary and essential factors of determination.' [1]

Wilson's matured view with regard to the influence of the chromosomes on development is in fact not so very different from that which is advocated here.

'We here again emphasize', he writes, 'the conception that the cell is a reaction-system and that the whole cell-system may be concerned in the production of every hereditary trait. In practice all the purposes of experimental analysis are sufficiently met if the hereditary "units", "genes" or "pangens" be thought of merely as modifiers which call forth responses, this way or that, according to their specific nature. To speak of them as "determiners" is to make use of a convenient figure of speech; but this need imply no more than that they are differentials by the use of which we are enabled accurately to analyze the observed results.' [2]

That chromosome differences act as modifiers of the general course of development is the conclusion at which we have ourselves arrived in the foregoing discussion.

A word or two more about the functions of the chromosomes. It would seem that they are best regarded as embodying particular modes of metabolic activity, as being the stable producers of particular chemical substances, such as enzymes or hormones, which are all-essential for the life, growth, and differentiation of the organism.[3] The fact that

[1] 1925, p. 1039. [2] 1925, pp. 1113–14.

[3] Cf. D. Noel Paton, 'The chromatin must be considered as an anabolite of protoplasmic activity, an anabolite transmitted from one generation to another, but even

they are walled off from the cytoplasm in the interkinetic phase when they are in a sol state, and are divided with such meticulous accuracy in their gel phase at mitosis, suggests that it is highly important they should be preserved essentially unchanged from one cell to another, and from one generation to the next. They may represent therefore the conservative element in the cell—the part which does not materially alter in spite of cytoplasmic differentiation. If this be so, they have some claim to be regarded in a general way as important for the maintenance of specific type, of specific modes of metabolism. Nuclear continuity or identity becomes from this point of view one of the most important *conditions* of that repetition of type which we call heredity. As Gates put it: 'The chromosome, as the most conservative body in the cell, thus makes possible the phenomena of heredity.'[1] The chromosomes may do this while not being in any sense the full determiners of hereditary characters, nor consisting of genes or determinants, or any other hereditary units. 'The autogenetic particles which it [the chromosome] is assumed to contain tend with increasing knowledge to lose their "representative" character and to become more purely chemical aggregations' (ibid., p. 500). A biochemical or physiological interpretation of the facts of Mendelian inheritance is probably not far off. It will come when the physiological functions of the chromosomes are better understood, when more is known as to the function of the nucleus in the cell, and as to the effect of the nuclei as a whole on the general metabolism of the body. It may well be that a study of the kinds of effects produced by modifications of single chromosomes, or of special loci of single chromosomes, as revealed by genetic experiment, will throw much light upon the main physiological functions of the chromosomes. For what we see in mutation are merely the incidental effects of

in the germ-plasm augmented in each generation. In its increase and in its distribution it follows the course of hereditary inertia, and its action in each generation may be (1) to stimulate the chemical changes that lead to division and multiplication, and (2) to stabilize the direction of chemical change which determines development on ancestral lines', *The Physiology of the Continuity of Life*, London, 1926, pp. 63–4.

[1] R. Ruggles Gates, in *Nature*, vol. cxv, 1925, p. 500.

slight but definite changes in chromosomal metabolism, but from these minor effects it may be possible to gain some inkling of the major functions of the chromosomes, both as a set and as individuals. An interesting line of study is here indicated.

Our conception of heredity and development as functions or activities of the whole unitary organism, which cannot be fully accounted for by the effects produced by its separate cells, or ascribed to the separate action of its nuclei, makes, as we have seen, the concept of a determinative germ-plasm, or internal formative mechanism, entirely superfluous. The germ-plasm theory was already on its last legs when it was given a new lease of life by the theory of the gene. Now this also is becoming physiological, and we shall soon have heard the last of both these abstract and morphological concepts.

We have seen in our historical survey of theories that the unity school has always maintained, in opposition to the particularist doctrine, that the germ-plasm is a superfluous fiction, and we have quoted several writers to this effect. We may here refer to two more, one from the botanical, the other from the zoological side.

F. Noll, in a remarkable series of papers published in 1903,[1] points out how the chief theorists have tried to solve the problem of development by assuming a material and particulate basis, without however attempting to explain how the mere presence of material elements could exert a controlling influence on development. They have been forced indeed to ascribe to such abstract material units properties and powers with which they would hesitate to credit the cell as a whole. They have thought of the characters of the adult organism as being represented in the nucleus by material particles, and have conceived it necessary to assume a sort of 'infection' by these particles of the generically indeterminate egg-cytoplasm in order to explain the visible phenomena of development (p. 323). But the concept of material representative particles is quite unnecessary. 'If the egg-cell of a

[1] F. Noll, 'Beobachtungen und Betrachtungen über embryonale Substanz', *Biol. Centralblatt*, xxiii, 1903, pp. 281, 321, and 401.

lime tree is already a young lime tree, there is no need of any idioplasm, germ-plasm, pangens, or heredity-substance to render possible its development into a lime tree; the egg-cell *as a whole* is the heredity-substance' (p. 325).

Our second illustration of the unity view is taken from Brachet, who writes:

'We have not considered it necessary, in the course of our discussion, to use the expressions "germ-plasm", "idioplasm" or the like, borrowed from the phraseology of Weismann, Nägeli, O. Hertwig and other theoricians of heredity. So too it has seemed to us unnecessary to discuss the question as to whether these substances, which are supposedly the material basis of hereditary tendencies, are represented by the chromatin of the chromosomes or by the mitochondria of the cytoplasm. As we have already said before, we consider with Delage, Conklin, Godlewski, Prenant and many others, that there is no one morphological substratum of heredity, any more than there exists, in the sexual cells or others, a substance of which it is the specific attribute. Heredity finds its total expression in the physical and chemical composition of the cells. It manifests itself in all the activities of life, from fertilisation right up to death, by the special turn it gives to these activities in each species and even in each individual. All the parts of the egg are necessary in order that the potentialities it contains may be harmoniously realised; all the substances play their part in this process, whether they exist in the form of organs or "organites" (nucleus, mitochondria, etc.) or in a state of ordinary or of colloidal solution.' [1]

Or again, explaining in the last pages of his book why he has paid no attention to the particulate theories of development and heredity:

'Without exception the authors of these theories: Darwin, Nägeli, de Vries, Weismann, O. Hertwig, to mention only those in the front rank, have thought it necessary, in order to explain heredity, i.e. the properties of the egg, to imagine the existence of special particles or substances to which they have given various names and whose structure even they have in some cases guessed at. For our part we do not see the need for these complications. We believe that the gemmules, pangens and other formed idioplasms, invented by these authors, give only the misleading appearance of an explanation, and

[1] 1917, pp. 187–8.

prejudge as to structures which have not been observed and, in some cases at least, cannot and never will be observed.'[1]

The view which we have worked out in this book—that the egg is from the very beginning the organism-to-be—is very similar to that advocated by Noll and Brachet, and like their theories renders a germ-plasm superfluous. We ourselves prefer to state this view in its organismal form, maintaining as we do that the concept 'organism' is more concrete and more adequate than the concept 'mechanism' or 'physico-chemical system'.

The integrative view may however be stated also in terms of mechanism, if the developing organism be regarded as being from the beginning a unitary system, which increases in size and degree of differentiation. The important thing is that the developing organism shall be considered primarily as a unitary whole, and not as a mere composite of parts.

One objection may be raised to this jettisoning of the germ-plasm theory which is worth some consideration. If there is no specific substance of a complex and definite organization which is responsible for heredity and development, how does it come about that development is so extraordinarily specific, and the repetition of type so extremely exact in every detail? Does not this point to a high degree of original preformation in the egg? The answer to this objection is given in principle by a remark of Delage, to which we called attention when discussing his views (see above, pp. 80–3). He points out that it is only necessary to assume that the egg has a very *precise* organization, a very exact and specific total structure, in order to account for the specificity of development. We need not assume any extremely elaborate preformation in the egg—to do so is merely to beg the whole question, and to put into the egg what is not actually there, namely the characters of the embryo and adult which develop from it. Insistence on the need for elaborate pre-organization in the egg is indeed merely a confession of weakness on the part of the intellect, which

[1] 1917, pp. 312–13.

finds it difficult to conceive how from the relative simplicity of the egg there develops the enormous complexity of the adult.

The exact repetition of type by the minute living egg is indeed an amazing thing, and it may never be fully explicable, but there is no need to imitate the old preformationists and adopt in despair the view that because we cannot understand development there is in reality no development, but merely an unfolding of complexities already present in the egg invisibly.

That the nucleus plays an important part in maintaining stability of type we have seen to be highly probable. If the nucleus represents essentially the conservative element in the cell, as the bearer of certain fundamental metabolic rhythms and the producer of certain essential enzymes and hormones, the fact that its continuing identity is accurately conserved by its exact division in mitosis indicates one means by which precise repetition of type is favoured. Another way in which the exact specificity of development is furthered may be the transmission of specific proteins. There is much evidence that allied species differ from one another in respect of their proteins, and these differences, though slight, are perfectly definite and stable. It is quite possible then that the differences between the eggs of two allied species may depend in part, but only in part, on the differences between the proteins of which they are respectively built up, and that in general the specificity of development may, to some extent and in some respects, be due to the specific nature of the proteins involved.[1]

8. One of the most potent ideas which the genius of Weismann imposed upon his contemporaries was the conception of the separateness and distinctness of somatic and germinal cells. The latter, containing the full hereditary equipment of the germ-plasm, lived an isolated and independent life in the midst of the somatic cells, which, having become specialized through the qualitative disintegration of the Id, were no longer capable of reproducing the species. The contrast between the immortal germ-plasm, enshrined

[1] See the views expressed by Loeb and R. S. Lillie, pp. 88–9 above.

in the germ-cells, and the fugitive somatic plasm, was regarded as absolute. The individual organism was looked upon as passing and evanescent—as it were a mere temporary shoot from the continuous stolon of the germ-plasm. On such a conception, the value and importance of the individual was hardly apparent, save as a means of protecting and nourishing the germ-plasm. Nor was it clear on the pure germ-plasm theory why the germ-cells must undergo a long process of maturation before they become capable of reproducing the species.

Under the influence of the Weismannian conception, much attention was devoted to tracing back the germ-line (Keimbahn) to the earliest stages of segmentation, and to demonstrating wherever possible an early segregation of the germinal cells. On the modern view of the germinal substance, conceived as having its seat in the chromosomes and as being exactly divided quantitatively and qualitatively in every mitotic division, Weismann's conception of the separateness of germ-plasm and somatic plasm is seen to have no foundation in fact. The 'germ-plasm' is present unaltered in every cell of the body, and, theoretically at least, every nucleus contains the complete potentialities for the development of a new individual. It follows then, to put the matter somewhat crudely, that the only difference between somatic cells and germinal cells must be a difference in their cytoplasmic organization.

It is an interesting fact in this connexion that in certain cases, where the germ-track can be followed right back to the egg, the determining factors for the primitive germ-cell are cytoplasmic. Thus in *Ascaris* the experiments of Boveri have shown that the difference established at the 4-cell stage between somatic cells with diminished chromatin and the primitive germ-cell with the full complement of chromatin depends on a cytoplasmic differentiation.[1] So too in some insects where the germ-cells are early differentiated the conditioning factor appears to be a cytoplasmic body, the so-called germ-cell determinant.

[1] See Wilson, 1925, pp. 1091–2.

It seems quite certain that there is no such thing as an unequal division of the nucleus, leading to differences being established between nuclei in respect of their composition and potentialities, and hence that there can be no distinction between germ-cells and somatic cells, so far as their nuclei are concerned. It is of course a definitely established fact that cells recognizable as primitive germ-cells are in many forms early set apart and cut off from the differentiations characteristic of the cells of the body. They pursue an evolution of their own, which culminates in their becoming mature ova or mature spermatozoa. This evolution is largely a cytoplasmic one, and results in the formation of two extreme and highly specialized types of cell. There is therefore solid ground for drawing a general distinction between germ-cells and somatic cells, quite apart from any theoretical considerations.

But this distinction also is no absolute one. The germ-track is often well defined, and may show direct continuity from the primitive germ-cells to the mature gametes; but the track can be interrupted, and germ-cells may arise *de novo*. Cases are certainly known where, after the complete elimination of the original line of germ-cells, new germ-cells have been formed from undifferentiated or dedifferentiated tissue cells. Two instances may suffice in illustration.

In his studies of regeneration in *Planaria*, Morgan [1] found that head-ends cut off well in front of the reproductive organs could develop into complete individuals which formed new reproductive organs. One of these examined by means of sections was found to be normal in every respect and to have well developed ovaries; others actually laid eggs. This result shows 'that new germ-cells can develop from the somatic tissues, or at least from cells not included in the old reproductive system' (p. 186).

Our second instance relates to the mouse. Davenport [2] has

[1] T. H. Morgan, 'Growth and Regeneration in *Planaria lugubris*', *Arch. Ent.-Mech.* xiii, 1902, pp. 179–211.

[2] C. B. Davenport, 'Regeneration of Ovaries in Mice', *Journ. Exper. Zool.* xlii, 1925, pp. 1–12.

recently shown that when the ovary in this form is completely removed a new ovary may regenerate from the remains of the stalk or even from the peritoneum.

G.T.Hargitt,[1] who has given much attention to the origin of the germ-cells in Coelenterates and other forms, well expresses the modern view of the relation of germ-cells to body-cells as follows:

'The dedifferentiations of cells, the probable origin of vertebrate germ cells from a new production following degeneration of primordial cells, the formation of germ cells whether primordial or definitive from such tissues as the peritoneum, the absence of demonstrable evidence of a specific germ track in Weismann's sense—all these point to the view that germ cells are as much differentiated from the embryo as are other tissues and cells. . . . It would seem proper and logical, therefore, to discard our previous views of the difference between body cells and germ cells, and the complete isolation and insulation of the latter from the influences of the body, even to discard the concept of the germ plasm and its continuity, since the germ plasm (nucleus) is equally present in every cell of the body, and the germ cells are no more continuous with the egg than all other cells' (pp. 92–3).

We see then that the distinction between germ-cells and somatic cells, though real, must not be pressed too far; both are the result of differentiation, along two different and divergent lines.

This question of the origin and differentiation of the germ-cells leads us naturally to the consideration of reproduction, which must be regarded as one of the master-functions of the organism, and as in a sense the crown and aim of development.

9. Like development, reproduction has been looked at too much from the cellular point of view, and too little from the point of view of the organism as a whole. It is one of the main activities of the living thing, and its influence on the whole being of the organism is profound and far-reaching.

How then shall we regard reproduction from our synthetic

[1] 'Germ-Cell Origin in the adult Salamander, *Diemyctylus viridescens*', *Journ. Morph. Physiol.* xxxix, 1924, pp. 63–111.

or organismal standpoint? We have got rid of the germ-plasm hypothesis; and we have seen that development is not merely a cellular process, but requires for its understanding the concept of the organism as a whole. Unhampered by the preconceptions of the cell-theory and the germ-plasm theory, we are in a position to look on reproduction in a different light, and in particular to bring under one general concept both sexual and asexual reproduction.

It is to K. E. von Baer that we owe the essential definition of reproduction, which will serve as a guide to our discussion, namely *the taking on by a part of the potentialities of the whole* (see above, p. 36). In reproduction, a part, be it egg or bud or fragment, escapes as it were from the domination or control of the whole, and develops a new individuality. This definition is comprehensive enough to cover all the modalities of reproduction.

Let us consider first asexual reproduction. Confining our attention to the animal kingdom, we may distinguish the following main types of asexual reproduction, namely, (1) division into two, as in many Protozoa and in some Metazoa, (2) the splitting off of fragments, as exemplified by some Actinians, (3) budding and strobilization as in some Coelenterates and worms, (4) sporulation, or the formation of unicellular or multicellular spores.

Of these, division into two is the simplest, and will afford us an insight into the essential nature of asexual reproduction. Let us follow what happens in the reproduction by fission of a highly organized Ciliate, such as *Stylonichia*. The process is described by Fauré-Fremiet[1] as follows. In the very first stage of division, even before the coming of fission is indicated by a constriction of the body, new ciliary elements appear. These are four supplementary rows of marginal cirri, two anterior and two posterior, one on the right side of the peristome, below the lateral cirri, the other below the peristome, between the abdominal cirri; a new peristome finally is formed to the left, below the old one, in a sort of intracytoplasmic cavity. Later the new peristome opens to the

[1] E. Fauré-Fremiet, *La Cinétique du Développement*, Paris, 1925.

exterior, with its fringe of adoral membranellae and its two undulatory membranes, endoral and paroral; then a constriction of the body indicates the coming separation of two individuals. 'It is remarkable to observe that at this stage, if we regard the extremely exact disposition of the vibratory apparatus, *three forms are superimposed* on the same protoplasmic body; the form of the original individual, preserved almost entirely, and those of the two new individuals, interwoven with it. At the later stages, the cirri of the original individual, shared between the two daughter-cells, disappear, and new cirri take their place' (pp. 20–1). The important thing to note is that there is not merely or principally a division of the existing organization into two, but a reorganization of the whole, including the reconstitution of two complete new individuals. The parts become wholes, even before separating from each other.

Such a process of reconstitution is common among Protozoa of a certain degree of complexity. There is generally some amount of dedifferentiation as a prelude to the redifferentiation of the two daughter-cells. In Flagellates, writes Calkins,[1]

> 'Reorganisation is indicated to some extent by those cases in which the old flagellum is absorbed. It is also evident in those forms of Chrysoflagellida, Cryptoflagellida and Euglenida which reproduce in the palmella or quiescent phases after the exudation of a gelatinous matrix, and after loss of the characteristic swimming organs. It is still better indicated by a number of flagellates in which the cytoplasmic kinetic elements, as well as the flagella, are all absorbed and replaced by new combinations in each of the daughter cells' (p. 210).

Reconstitution of wholes from parts is most marked in Ciliates—'The processes through which the ciliate cell passes during division indicate that the organism is restored to a generalized condition practically equivalent to an encysted cell. Except for the cytostome the entire array of complex cortical organs is withdrawn and a new set is formed from the cortical protoplasm' (p. 223).

Now exactly the same process of the reconstitution of a

[1] G. N. Calkins, *The Biology of the Protozoa*, London, 1926.

new whole from a part of the original organism takes place in the asexual reproduction of Metazoa. When *Hydra* forms a bud, or the scyphistoma of *Aurelia* cuts off successively little medusae, or a detached fragment of *Sagartia elegans* grows into a new individual,[1] there is the same reconstitution of a new whole from a part. The fact that in the Protozoa the process is carried out within a single cell, and that in the Metazoa many cells are concerned in forming the new individual, may be regarded as purely secondary, and as being in the main a dimensional difference.

The point is well put by Whitman:[2]

> 'In the infusoria we see most complex organizations worked out within the limits of a single cell. We often see the formative forces at work and structural features established before fission is accomplished. Cell-division is here plainly the result, not the cause, of structural duplication. The multicellular Microstoma behaves essentially in the same way as the unicellular Stentor, or the multinucleate Opalinopsis of Sepia. The Microstoma organization duplicates itself, and fission follows. The chain of buds thus formed bears a most striking resemblance to that of Opalinopsis, and the resemblance must lie deeper in the organization than cell-boundaries' (p. 115).

In the same way, there is a close analogy between the unicellular spores produced by many Protozoa and Protophyta and the multicellular 'spores' of some Metazoa and Metaphyta, e.g. the gemmules of Sponges, and the gemmae of Liverworts; these are all parts separated from the whole, which have acquired the potentiality of reproducing the whole.

Brachet, who discusses in an interesting manner the question of asexual reproduction, sums up the general characteristics of this type of reproduction as follows:

> 'At a given moment, and under the influence of conditions which must be determined in each particular case, one or more parts of the body of an organism—Protozoon or Metazoon—cease to function in

[1] T. A. Stephenson, 'On the Methods of Reproduction as Specific Characters in Sea Anemones', *Journ. Mar. Biol. Assoc.* xvi, 1929, pp. 131–72.

[2] C. O. Whitman, 'The Inadequacy of the Cell-Theory of Development', *Wood's Holl Biol. Lectures for 1893*, Boston, 1894, pp. 105–24.

their usual way and manifest properties, if not new at least unsuspected hitherto; they abandon the role assigned to them by their position in the organism to take up functions of an autogenetic origin which are infinitely more complex—the building up, by themselves, of a new individual, similar to the original one.'[1]

This manifestation by a part of a hidden power to produce the whole, whether it be a part of a monoenergid or of a polyenergid organism, Brachet, following Child,[2] connects up with its physiological isolation, however caused, from the general vital processes of the parent organism. We see the effects of isolation most clearly in cases where a part is separated mechanically from the whole and regenerates the whole.

Particularly suggestive are those numerous cases of regeneration where the separated part, instead of merely adding to and completing its structure, undergoes dedifferentiation and reorganization, remodelling its structure so that from the part there is formed, without any growth or cell-multiplication, a new individual of reduced size, by the process named by Morgan morphallaxis. As instances may be adduced the formation of tiny but complete individuals from small sections of *Planaria*, the reorganization of pieces of *Tubularia*, and the reconstitution of whole *Clavellina* from cut up pieces of the original whole. The same process of reconstitution of parts occurs in the regeneration of unicellular organisms. Apropos of such experiments, Morgan's[3] remarks are worth quoting:

'Numerous experiments on *Protozoa* and *Protophyta* have shown that a nucleated part is capable of forming a new individual. So far as we can see there is not in most cases, perhaps in none, the formation of new indifferent protoplasm in which the new parts are developed, but the entire piece is changed over into a complete animal or plant of smaller size. At first sight there seems to be here a marked difference between the regeneration of unicellular and multicellular forms, for

[1] 1917, p. 29.

[2] C. M. Child, *Die physiologische Isolation von Teilen des Organismus als Auslösungsfaktor der Bildung neuer Lebewesen und der Restitution.* Roux's Vorträge, xi, Leipzig, 1911.

[3] T. H. Morgan, 'Some Problems of Regeneration', *Wood's Holl Biol. Lectures for 1898*, Boston, 1899, pp. 195–207.

in the latter it is usual for a knob of new tissue to appear, and out of this the new part develops. However, Trembley saw that when a *Hydra* is cut longitudinally the cut edges bend in and fuse, forming a new tube of smaller diameter. Nussbaum has also observed in *Hydra* the rolling in and fusion of the cut edges. In both cases the new form develops without the previous formation of new tissue. In a tubularian hydroid Bickford has found that when a piece is cut from the stem the new tentacles appear in the old tissue, and I shall describe more fully below the results of some experiments on planarians which show that the old part plays an important role in the formation of the new individual. We see then that the difference between unicellular and multicellular forms is not so great as appears at first sight. . . . Do not these cases of regeneration in the multicellular form indicate that the individual is a whole in the same sense that the unicellular form is a whole?' (p. 196).

10. Sexual reproduction differs from asexual only in the fact that the origin of the new individual is a single cell, and that in this egg-cell, after the process of fertilization, half the chromosomes are of paternal, half of maternal, origin.

As a form of reproduction it is widespread throughout the organic realm, and it is undoubtedly of greater general significance than asexual reproduction. It results as a rule in the production of a much greater number of new individuals, and it is clearly a process economical of substance and energy in proportion to the number of new individuals started in life. Natural parthenogenesis is clearly derivative from ordinary sexual reproduction.

Apart from the two differences mentioned—unicellular origin and fertilization—there is however, as we shall see, the closest analogy between sexual and asexual reproduction, for in both the essential process is the redifferentiation of a part so that it becomes both potentially and, later, actually a whole.

All experimental work goes to show that sooner or later during the process of segmentation, according to the degree of original cytoplasmic prelocalization, all the cells lose their power to reproduce the whole when separated from their neighbours. Sometimes this power is lost at the very first division, or it may persist in certain cases till the 16- or 32-

cell stage, but in no case is it retained for very long. It is clear then that if this power is lost by the segmentation cells it must be re-acquired by the cells which give rise to the ova, for the ova are essentially characterized by their power to reproduce the whole. There must therefore occur, just as in asexual development, a reconstitution or remodelling of a part or parts in such a way that these parts re-acquire the potentiality of forming a new whole. The difference between the two processes is mainly one of scale or dimensions; the bud or segment or part in asexual reproduction is usually polyenergid and of a certain size, while the ovum is as a rule relatively small (apart from its stores of yolk) and is invariably monoenergid. Even this difference disappears if we consider asexual reproduction by fission in Ciliates, where the part which is reconstituted a whole is small and monoenergid. As compared with the state of affairs in Ciliates, the process of egg-formation in Metazoa differs merely in the fact that the parts separated off are usually very numerous, and are almost invariably minute in comparison with the large polyenergid body of the parent; further, redifferentiation of structure and the re-acquirement of the potentiality to form a whole occur in Metazoa *after* the separation of the parts as primitive germ-cells, but to some extent *before* division or separation in Ciliates. But essentially, from the organismal point of view, the two processes are the same, and the differences relate to unimportant details. The egg may therefore be considered as equivalent to a uni-cellular bud.

It will be remembered that in Chapter I we indicated that the main characteristic of differentiation was the progressive limitation of the potentialities of the parts formed during the course of development. Functional differentiation entails physiological division of labour and a loss by the differentiated parts (cells or organs) of the more general potentialities possessed by the egg. The germ-cells constitute in some measure an exception to this law, for they have re-acquired and preserve this original total potentiality, which was possessed by the egg-cell from which they are derived.

Brachet expresses this general difference, between the

differentiated tissue cells and those cells and groups of cells that have re-acquired the potentiality of the whole, in terms of the 'specific composition of the egg-protoplasm', as follows:

'Modified at the very first segmentation, but often capable of re-establishing itself in the two daughter-cells if their connection is broken, able to repeat the process, under the same conditions, in the four blastomeres formed from the first two divisions of the egg, capable of reconstitution sometimes, in certain privileged cells, at more advanced stages, this composition is lost to an increasing degree in proportion as differentiation progresses. But it is evident that it is not altered at the same time and to the same extent in all cells or in all groups of cells. There are some cells which, by reason of their origin, will very early diverge from the fundamental composition of the species-protoplasm; the connections constantly renewed which become established between them and their neighbours, the special character of their metabolism, determined by the position they occupy, and the effect of their correlations, will create in them functional structures which rapidly become fixed and indelible. This is the case for example with the nervous system in all Metazoa.

'On the other hand, in other more favoured groups of cells, the imprint of correlations, being less accentuated, will leave open the possibility of a return to the initial stage,[1] which, being the normal state, typical of the species, must have a natural tendency to re-establish itself as soon as favourable conditions allow. There enter into this category without a doubt the mother-cells of the sexual products, the elements that form buds, gemmules, statoblasts, etc.'[2]

It is interesting to note that Brachet states the matter also in terms of potentialities, just as we do—actually of course 'specific composition' and 'total potentiality' are equivalent expressions for the same thing. Thus he writes:

'If the real and total potentialities of blastomeres and of the groups of cells which are derived from them were known at all stages in the development of an organism, we could predict with a high degree of probability the "virtual" or "latent" properties of the different tissues and organs of the body. One could enumerate in advance those which have produced all they are capable of, those which are capable of regeneration and to what degree, those which can form

[1] Cf. Delage, p. 79 above.

[2] 1917, pp. 308–9.

buds or gemmules, and those finally which are capable of becoming sexual cells.'[1]

Along such lines, by the use of such concepts, a rational analysis of development seems possible.

Accepting as he does, to a very considerable degree, the organismal conception of development and reproduction, Brachet naturally lays emphasis on the essential similarity between sexual and asexual reproduction; for him, as for us, reproduction is essentially the taking on by a part, whether monoenergid or polyenergid, of the characters of the whole.

The same view is expressed by Child, who as we have seen (p. 92, above) is no believer in the classical theory of nuclear determination, which is so completely opposed to the organismal conception. In his remarkable book, *Senescence and Rejuvenescence*,[2] he writes:

'We can dispense entirely with that remarkable conception, the germ plasm of the Weismannian theory, and say that germ plasm is any protoplasm capable under the proper conditions of undergoing dedifferentiation and reconstitution into a new individual of the species. Reproduction, whether it is the process of reconstitution in a piece experimentally isolated from an animal or plant body, or the process of development from the fertilised egg, is fundamentally the same physiological process and involves both regressive and progressive changes, both rejuvenescence and senescence' (p. 427).

Summing up our discussion at this stage, we may say that both the ovum and the bud (using the word in its widest sense) are parts of the organism which re-acquire that potentiality of forming a whole which in the first stages of development is lost by the cells and parts of the parent organism. From the organismal point of view it is comparatively unimportant that the one is monoenergid, the other polyenergid, for both are new *organisms* in their simplest, most undeveloped state.

In the fly *Miastor* the larva produces by parthenogenesis a number of viviparous young. It is hardly fanciful to see in this an actual case of budding, differing from ordinary internal budding only in the fact that the bud or embryo

[1] 1917, p. 310. Cf. Child, p. 92 above. [2] Chicago, 1915.

originates from a single cell. Actual budding of parts from *groups* of undifferentiated cells is exemplified in the development of the imaginal disks in holometabolic insects.

It is possible that sexual reproduction by means of single cells (which differentiate as organisms at first within the limits of the single cell) is historically a specialization of development from a primitive mode of asexual reproduction by fission or budding. It has many advantages over the latter, and it permits of that mingling of paternal chromosomes in the nucleus of the egg which clearly has some deep significance, judging from the predominance of sexual development, though what that significance may be is not yet fully clear.

11. Reproduction, or the formation of a new individual, begins when a cell, or a number of cells, or in unicellulars a portion of a cell, ceases to behave as a part and takes on progressively the characters of a whole. The development of ova therefore, regarded as the future individuals, begins long before they are mature, and long before they are fertilized and commence embryogeny proper. In a sense therefore, all organisms producing eggs are viviparous, even though fertilization and further development may take place outside the body of the parent, for the egg is already the beginning of the new organism.

At the same time, the production and ripening of germ-cells may be regarded as the final term and completion of the development of the parent organism. Hence the development of the parental generation overlaps the development of the filial generation. We have to picture then not a continuous lineage of germinal cells, giving off at intervals shoots representing successive generations, successive flowerings of the germ-plasm, but an actual new production in each generation of the generation to come. As Samuel Butler said, the hen on this view does actually make the egg and the chick, and the chick in the fullness of time makes another egg, just as its mother did before it.[1] It is in this way that we

[1] The same view is held by A. Cohen-Kysper, 'The germ-cell also reconstitutes itself. It returns again to the same orderly determined state in which it began its

must conceive the continuity of life—it is a continuity passing *through* the individuals of each generation, not an abstract continuity separate and apart from the lives of individuals. Eggs are parts of organisms which become reconstituted as wholes, just as buds do; they are not mere links in an endless chain of germ-cells transmitted unchanged from generation to generation.

From the organismal point of view, the long maturation which eggs must undergo before they can be fertilized and start embryogeny becomes understandable. It is not understandable on the germ-plasm hypothesis. If the nuclei of the primitive germ-cells—or for that matter the nuclei of any other type of cell—contain within them all the determining factors of development, why is it that they do not develop straight away? And if it is averred that the cytoplasmic maturation of germ-cells is the work of their nuclei, of the internal and invisible mechanism of the genes, pangens or what you will, why is it that tissue cells, which contain the same complement of heredity units, do not normally manifest this reconstitution as wholes? The period of maturation is essentially taken up by the long process of reconstitution whereby from a cell that commences as a part of the organism there is developed a new if embryonic whole.

It may be noted in passing that this life and development of the ova in the heart of the maternal organism enables them in a measure to share in the life and experience of that organism. It is true that the trend of their evolution is different from that of the tissue cells, and that they live to some degree a life apart, but the possibility cannot be excluded that they may be altered insensibly by the vicissitudes through which the mother passes, and there is here at least a slight opportunity for the transmission to the germ-cells of peculiarities acquired by the parent during the time they form part of her body. It may be difficult to conceive how the experience of the organism as a whole may be shared in by the germ in such a way as to become manifest in the course

development' (p. 18), *Kontinuität des Keimplasmas oder Wiederherstellung der Keimzelle.* (Vortrag) Leipzig, 1923, 24 pp.

of its later development, but transmission at a lower level at least is easily comprehensible. One might expect that any radical alteration of the metabolism of the parent would be shared in by the germ-cells, which are bathed by the same *milieu interne*, and are subjected like the 'somatic' cells to the influence of the various substances dissolved therein. Direct effect at the chemical level on 'soma' and germ-cells alike, or on the germ-cells through the intermediary of the body-cells, has been often demonstrated. One need only mention in illustration the results obtained by Heslop Harrison on the artificial production and transmission of melanism in moths.

Coming back after this digression to consider in more detail the maturation of the primitive ova—we have already noted that germ-cells start from an undifferentiated or dedifferentiated state and undergo a long process of redifferentiation. The mature germ-cell is a highly differentiated cell.

So far as the female gamete is concerned, this differentiation shows a very special character. Much of it is to be interpreted as a preparation for the future embryogeny. In some cases there is, as we have seen, an actual building up of a cytoplasmic organization which foreshadows in its main lines, though in the broadest way, the organization of the future embryo; this preformed organismal structure, however, is not as a rule completed until the spermatozoon enters. But there is during the evolution of the ovarian egg a preparation for the assumption of the 'organism-structure' which characterizes the mature and fertilized egg. It is noteworthy by the way that the prelocalized areas of the fertilized egg are usually so arranged that on gastrulation they fall into their proper positions and relations in the developing embryo—this also is anticipatory development.

Another process which obviously takes place in the cytoplasmic maturation of the egg, and is clearly preparatory of the future, is the accumulation in the egg of the yolk and other materials necessary for the maintenance and growth of the early embryo. This is a process comparable, as Aristotle saw, with the formation of milk in the mammary glands

of the Mammalia, in advance of, and in preparation for, the needs of the coming offspring. Both are typical cases of anticipatory action or anticipatory response.

Child, who has emphasized the point that the mature ovum is highly differentiated, though along different lines from the tissue cells, considers that it is essentially a senescent cell, which becomes rejuvenated through natural or artificial fertilization. Certain it is that towards the end of its cytoplasmic maturation the egg is a singularly inert and quiescent cell, with an abnormally large nucleus or germinal vesicle, and a cytoplasm often loaded and swollen with deutoplasmic material. It may perhaps be regarded as a cell which has reached the term of its development *as a cell*, and as being in this sense senescent. It has however vast potentialities dormant in it, which can be released or awakened by many means, natural or artificial. Activation of the egg must be regarded as the removal of the bar, whatever it is, that prevents the egg from developing farther—whether by overcoming its impermeability, or by remedying the state of semi-asphyxiation in which it is supposed by some to be, or by some other means. Segmentation, as we have seen, may be regarded as a process whereby the large and inactive nucleus of the egg is restored to activity by a division up into smaller units, which expose collectively a larger surface of action than the original whole nucleus. There is accordingly much to be said for Child's view that fertilization, or more generally the stimulus to development, leads to a rejuvenescence of the egg. But it must be remembered that the potentialities of the egg are there already, only inhibited from expressing themselves; the egg is not first endowed with them by the mere stimulus to development, a stimulus which may be purely mechanical, and is anything but specific.

12. In conclusion, let us consider very briefly the part played by the chromosomes in asexual reproduction. In discussing heredity and development generally, we saw that there might be distinguished various levels or grades of hereditary transmission. We reached the conclusion that the potentialities of the whole organism could be carried over or

transmitted only by that which is itself a potential whole, e.g. the ovum, and that they must be carried by the ovum as a whole. Parts of the whole could transmit only their characters and potentialities as parts, and there was, we saw, something artificial and abstract in considering the potentialities of the parts in isolation from the activity of the whole. The activities of the parts can never fully explain the activity of the whole; they are to be regarded rather as conditions, both limiting and implementing that activity. The chromosomes therefore in sexual reproduction cannot be the full and sole determiners of the characters of the egg, or of the embryo, or of the adult; they can only carry over their own modes of activity, which we found reason to believe are essentially particular modes of metabolic activity.

Exactly the same considerations apply to asexual reproduction. The potentialities of the bud are not represented by the organization of the chromosome complex in each of its cells; the developed characters of the bud are not determined exclusively or mainly by the chromosomes of its single cells, or even by the cells themselves. The bud *as a whole* has reacquired the potentiality of producing a new organism; the cells and their nuclei are conditions, not causes, of the realization of this potentiality. The chromosomes carry over into the new individual certain stable metabolic rhythms, certain stereotyped methods of chemical synthesis and chemical production, and represent thus a conservative element in hereditary transmission; they have nothing directly to do with the differentiation of the bud, beyond supplying the necessary means for growth. The unity of the new developing individual, the bud, has come into being somehow; we can probably discover the conditions which enable this unity to arise; but once it has arisen we must accept is as something *given*, and interpret the cell activities and chromosomal activities of the bud in this light, rather than attempt the hopeless task of explaining the unity of the developing bud in terms of the activities of its subordinate and abstract parts.

The general conception of reproduction to which we have been led by a simple application of the organismal method is

therefore quite different from that which arises from theories of nuclear determination. It is hardly necessary to enlarge on this point, which has already been dealt with repeatedly in the course of this book. From the organismal point of view, the existence of any form of germ-plasm, of any specific substance or organization determining heredity and development, appears not only an unnecessary hypothesis but a misleading and erroneous one. The germ-plasm theory has in fact outlived its usefulness, and is now become a hindrance to the proper understanding of development and heredity. These processes must be regarded primarily as activities of the whole organism, affecting the whole organism, and carried out by the whole. Nothing but confusion will result if we attempt to ascribe these processes exclusively to the activities of certain parts of the organism—cells or nuclei, chromosomes or genes. If analysis of the organism is undertaken—and its value in increasing knowledge is fully admitted—there must follow upon this analysis, the abstract character of which must be recognized, a vigorous attempt at re-integration, a determined effort to put back all the part-processes artificially isolated by analysis into their proper relations with the whole. A concrete and comprehensive understanding of development and heredity can be attained only be keeping steadfastly in view the essential unity of the organism which is manifested in these activities.

We have in a previous chapter discussed the differences between the integrative and the analytic view, and we have steadily maintained the indispensability of an integrative or organismal conception. In these last few chapters, dealing with the cell-theory, with the problems of early development, and with the general interpretation of reproduction, we have tried to show the value of this conception. We have done no more than illustrate its use; and there remains yet much to be done in applying it to the problems of later development, and indeed to all the other general problems of biology. May it prove fruitful, and lead to a better understanding of the abiding mystery of life.

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